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# Some metal-metal interconversions with organolithium compounds

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SOME METAL-METAL INTERCONVERSIONS  
WITH ORGANOLITHIUM COMPOUNDS

by

Fred Warren Moore

A Thesis Submitted to the Graduate Faculty  
for the Degree of

DOCTOR OF PHILOSOPHY

Major Subject Organic Chemistry

Approved:

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Iowa State College  
1941

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## INTRODUCTION

Organolithium compounds have become important tools in synthetic chemistry only in the past decade and although much is now known about these interesting and useful compounds, further studies are necessary before our knowledge of them and their reactions is adequate.

In a general way the organolithium compounds undergo several different types of reaction. These may be more or less arbitrarily divided into several types. First, they add to many multiple bonds in cyclic and open-chained molecules. Second, they give hydrogen-metal interconversion or metalation with many compounds. Third, they react with various organic halides to give halogen-metal interconversion. Fourth, they react with many other organometallic compounds by metal-metal interconversion. Fifth, some molecules are cleaved by organolithium compounds in reactions other than the interconversions mentioned. Sixth, they give coupling products with many substances. Seventh, some inorganic metal salts react with them. Finally, various other reactions, of lesser importance, take place.

Such a variety of reactions demonstrates not only the utility of the organolithium compounds but, also, the complexity of a systematic study of them. As is shown in the

Historical part, some of these reactions have been rather thoroughly investigated whereas others have received only scant attention. With this in mind, the present study was made in order to extend the knowledge of these lesser known reactions.

The following problems have been investigated:

1. Improvement of methods for preparing and utilizing various types of organolithium compounds, as well as the preparation and uses of hitherto unknown types such as that in which the lithium atom is attached to a tertiary carbon atom.

2. Determination of the important factors affecting halogen-metal and metal-metal interconversions involving organolithium compounds.

3. Comparison of the relative reactivities of the organolithium compounds used most extensively in some of the above-mentioned types of reaction.

These problems, overlapping to some degree as they must, are important in that possible correlations of relative reactivities in the various reactions will make possible the selection of optimum conditions and best reactants for certain syntheses with a minimum of trial and error studies, and may allow preferential reactions to be carried out with polyfunctional compounds.

The Historical part covers the literature up to January, 1941.

## HISTORICAL

A chronological history of the organolithium compounds is not desirable since such a treatment, embracing all the types of reaction shown by these compounds, would lead to confusion and needless repetition. A more desirable method, one which lends itself to a clear presentation more readily, is to separate the various types of reaction into several groups and discuss each as a unit. Such is the method used here, the reactions being separated as in the Introduction. Before that phase of the subject is discussed, however, a summary of the reactions between lithium metal and various hydrocarbons must be made in order to correlate an otherwise scattered mass of facts concerning an important class of organolithium compounds.

### Reaction of Lithium with Hydrocarbons

W. Schlenk and E. Bergmann have worked most intensively on the addition of alkali metals to multiple carbon bonds. The variety and complexity of their studies are appreciated only after a careful survey of their work. Although later investigations have shown that a few of their results are in error, on the whole they have done splendid work. This is further appreciated when it is realized that, because of

the very nature of the substances with which they dealt, the products they isolated were in some degree determined by the conditions of reaction and methods of characterization.

In general, the addition of lithium to carbon-carbon double and triple bonds is rather slow and often leads to a variety of products from a single reactant. Such changes as rearrangement, with or without cyclization, and polymerization often lead to a complex mixture of substances.

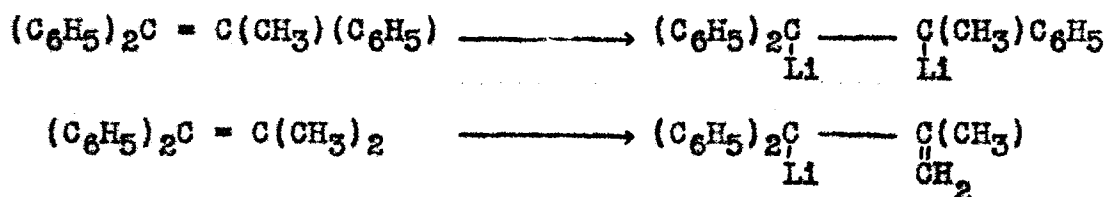
Addition to open-chained molecules.

Molecules containing a single ethylenic linkage conjugated with aromatic double bonds add lithium metal slowly in ether solution. 2,3-Diphenyl-2-butene (sym. diphenyldimethylethylene) and sym. diphenyldibiphenylethylene, when shaken with lithium in ether for three days, add two atoms of the metal (1). Hydrolysis of these addition compounds with ethanol yields the corresponding ethanes. Carbon dioxide converts the metal compounds into the corresponding substituted succinic acids. Shaking the addition compounds with mercury regenerates the starting materials by removing the lithium atoms. These reactions are illustrated below for sym. diphenyldimethylethylene. The substituted succinic acid produced by the carbonation of the lithium addition compound of sym. diphenyldimethylethylene is different from

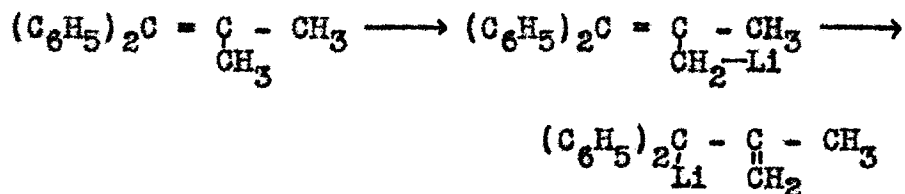
1. Schlenk and Bergmann, Ann., 463, 98 (1928).



diphenyl-2,2-dimethylethylene) apparently adds only one atom (3). Treatment of the addition product of the former with ethanol produces 1,1,2-triphenylpropane. The addition compound of the latter reacts with phenyl isothiocyanate to form the thioanilide of 2,2-diphenyl-3-methyl-3-butenic acid. The two reacting forms are apparently as shown:



Several possible explanations of the latter reaction can be made. One is the addition of two atoms of lithium followed by the elimination of lithium hydride. This possibility finds some support in the fact that ethyllithium splits out lithium hydride at higher temperatures (4). Another possibility is the metalation of one of the methyl groups by the lithium metal followed by allylic rearrangement either before or upon reaction with phenyl isothiocyanate.



This possibility is supported by similar rearrangement reactions of other organolithium compounds of this type, such as

3. Schlenk and Bergmann, Ann., **463**, 1 (1928).
4. Thomson and Stevens, J. Chem. Soc., 556 (1933).

benzylolithium (5). Unfortunately, sufficient data are not available to decide whether one of these or some other mechanism represents the true course of the reaction.

1,1,3-Triphenyl-1-propene (1,1-diphenyl-2-benzylethylene) also gives other than the expected 1,2-addition to the ethylenic linkage (6). In this case a mixture of products is obtained when characterization is attempted with various reagents. The products are somewhat analogous to those obtained from 1,1-diphenyl-2-methyl-1-propene. The addition compound reacts with benzyl chloride and, after hydrolysis, 1,2,2,4-tetraphenylbutane and 1,1,3,4-tetraphenyl-1-butene are found as the reaction products. With carbon dioxide the addition compound yields two acids, 2,4,4-triphenyl-3-butenic acid and 2,2,4-triphenylbutanoic acid. Phenyl isothiocyanate and the addition compounds form the thioanilides of these two acids. The resemblance to the above 1,1-diphenyl-2-methyl-1-propene is now clear and the possible reaction mechanisms suggested for that compound's reactions would apply equally well in this case. This mechanism, to form an equilibrium mixture of A and B, or a direct metalation to produce B, which then partially shifts to A (as indicated by end products obtained) would explain part of the reactions. It is seen that A and B are allylic forms. The obvious weakness in this conjecture is the fact that no adequate explanation of the formation of

5. Gilman and Breuer, J. Am. Chem. Soc., 56, 1127 (1934).

6. Schlenk, Bergmann and Blum-Bergmann, Ann., 479, 78 (1930).





radical, is probably the most logical of all the postulations. This mechanism assumes the formation of the normal 1,2-addition product which then reacts with unchanged starting material to give the same two organolithium compounds which were formed by the disproportionation of the above free radical. Although facts are known both in favor of and against each of these mechanisms, no definite conclusions can yet be drawn as to which is the true mechanism or whether one or a combination of several such processes is involved.

Ziegler and his coworkers have shown that lithium adds to 1,3-butadiene in ether solution but that only a tarry resin is produced on hydrolysis (8). 1,3-Pentadiene (piperylene) and 2,3-dimethyl-1,3-butadiene, however, form recognizable products (8). The former yields, along with other products, amylene and dihydrodipiperylene. The latter compound forms analogous products. Other substituted butadienes also give similar compounds. For example, trans, trans-1,4-diphenyl-1,3-butadiene adds lithium in ether solution (1). The action of ethanol on this addition compound forms 1,4-diphenyl-2-butene. Carbon dioxide produces the corresponding 1,4-dicarboxylic acid. Treatment with dry air or mercury regenerates the starting material.

Although 1,2-addition was the rule with the substituted ethylenes (see above) even though the ethylenic linkage was

8. Ziegler, Jakob, Wollthan and Wenz, ibid., 511, 64 (1934).

conjugated with the multiple bonds of aromatic rings, the longer chained unsaturated molecules do not yield products corresponding to 1,2-addition. The results with the above dienes and with other long-chained unsaturated compounds indicate that addition takes place at the ends of the open chain. The addition of lithium to such compounds as 1,1,4,4-tetraphenyl-1,3-butadiene (1), 1,2,4-triphenyl-1,3-butadiene (9), 1,6-diphenyl-1,3,5-hexatriene (10), 1,1,6,6-tetraphenyl-1,3,5-hexatriene (11), and 1,8-diphenyl-1,3,5,7-octatetraene (10) yields hydrolytic and carbonation products which seem to substantiate this addition to the ends of the open chain. It is apparent, however, that 1,2-addition followed by allylic rearrangement would also account for the formation of the products isolated.

9,10-Dibenzal-9,10-dihydroanthracene yields 9,10-dibenzyl-9,10-dihydroanthracene when it is treated with lithium in ether solution and the addition product is hydrolyzed (12). 9-Propenylphenanthrene, under similar conditions, is dimerized, 1,4-di(9-phenanthryl)-2,3-dimethylbutane being obtained on hydrolysis of the reaction mixture (9).

9. Bergmann and Bergmann, J. Am. Chem. Soc., 62, 1699 (1940).
10. Kuhn and Winterstein, Helv. Chim. Acta., 12, 493 (1929).
11. Wittig and Klein, Ber., 69, 2087 (1936).
12. Bergmann and Fujise, Ann., 480, 188 (1930).

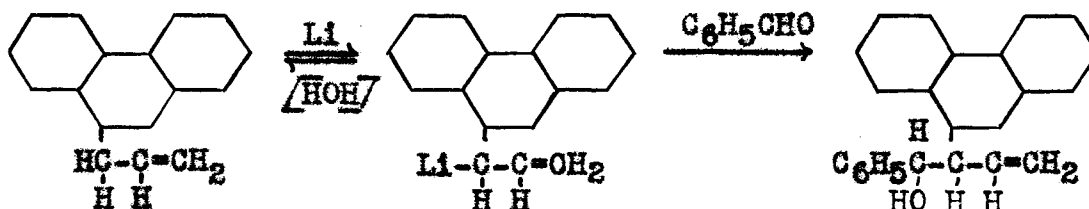
Addition and Cyclization.

Another type of addition of lithium to carbon-carbon double and triple bonds results in partial or complete cyclization. In many cases the products appear to be formed in rather complex reactions while in others quite simple reactions would account for the compounds obtained.

The simplest cases of cyclization are those involving compounds with a single ethylenic linkage. Thus, 1,1,3-triphenyl-1-propene (1,1-diphenyl-2-benzylethylene) when shaken with lithium in ether adds the metal and treatment of the addition product with benzohydril bromide, followed by hydrolysis, gives a mixture of products which includes tetraphenylethane and 1,3-diphenylhydrindene (6). The related 1,1-diphenyl-2-methyl-1-propene (1,1-diphenyl-2,2-dimethylethylene) after shaking with lithium in ether for four weeks was treated with benzyl chloride and then hydrolyzed. The products isolated were unchanged starting material, 1,1-diphenyl-2,2-dimethylethane and a hydrocarbon,  $C_{23}H_{22}$ , which was assigned two possible structures (13), namely: 1-phenyl-2-methyl-3-benzylhydrindene or 1-phenyl-2-(3-phenylethyl)hydrindene. No conclusive evidence of structure was obtained. 1,1,3,3-Tetraphenyl-1-propene after eight days in contact with lithium in ether yields, subsequent

13. Sehlenk and Bergmann, Ann., 479, 58 (1930).

to hydrolysis, 1,2,3-triphenylhydrindene (3). 9-Allylphenanthrene, in a similar manner, yields 9,10-cyclopentenophenanthrene (9). This behavior is in contrast to that of 9-propenylphenanthrene (see page 15) which gives no cyclization under the same conditions. The two compounds differ only in the position of the ethylenic linkage in the side chain. Treatment of the lithium addition compound of 9-allylphenanthrene with benzaldehyde does not yield a cyclic product but forms, instead, 1-phenyl-2-(9-phenanthryl)-3-buten-1-ol. The structure assigned to the lithium compound is based on the reaction with benzaldehyde, and on the fact that hydrolysis yields the original compound and not the reduced product usually obtained by hydrolyzing metal addition products. A

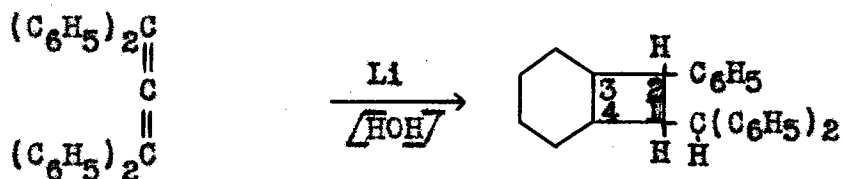


similar cyclization occurs when 2,2,4,4-tetraphenyl-3-butene is shaken with lithium in ether for six days and the reaction mixture is then hydrolyzed (14). The products obtained are 1-methyl-1,2,3-triphenylhydrindene, methyldiphenylmethane and isostilbene. Carbonation produces a 1,2- or 1,3- acid of the above hydrindene and also some 1,1,4,4-tetraphenyl-2-butene-1,4-dicarboxylic acid which evidently results from

14. Bergmann and Weiss, Ann., 480, 59 (1930).

the dimerizing action of lithium on the isostilbene formed in the reaction.

The reactions of compounds containing more than one ethylenic linkage with lithium also produce cyclic products in many cases. For example 1,1,3,3-tetraphenylpropadiene adds lithium in ether solution and, following hydrolysis, 1-benzohydryl-2-phenyl-3,4-benzocyclobutane is found as the reaction product (15). The mechanism of this reaction is



not clear. In like manner 1,2,3,4-tetraphenyl-1,3-butadiene adds lithium in ether to form a dark red-brown solution (16). Hydrolysis of this solution yields 1-benzyl-2,3-diphenylhydrindene along with some dibenzylstilbene. The action of metallic mercury on the metal compound forms 1-benzal-2,3-diphenylhydrindene. The tendency seems toward the formation of four-, five- and six-membered rings with the five-membered ring predominating, as might have been predicted from a general knowledge of ring closure. An example of the formation of a six-membered cycle is the case of 1,1,8,8-tetraphenyl-1,7-octadiene. Bergmann (17) treated

15. Schlenk and Bergmann, *ibid.*, 463, 228 (1928).
16. Bergmann, Winter and Schreiber, *ibid.*, 500, 122 (1933).
17. Bergmann, *Ber.*, 63, 2593 (1930).

this compound with lithium in ether for four weeks and then, after hydrolysis, was able to isolate substantial quantities of 1,2-dibenzohydrylcyclohexane. Wittig later showed (18) that in dioxane for three days, followed by hydrolysis, the products formed were sixty per cent of the cyclohexane derivative and thirty per cent of 1,1,8,8-tetraphenyloctane. This latter product indicates that metal addition to the double bonds precedes cyclization.

Molecules containing one or more acetylenic linkages have not been investigated to any great extent as regards their reactions with lithium metal. Diphenylacetylene or tolan, as it is commonly called, reacts with lithium in ether solution. Hydrolysis is accomplished with alcohol and a mixture of products is obtained. These products include 2,3,4-triphenylnaphthalene (3), 1,2,3,4-dibenz-9-phenyl-9,10-dihydroanthracene (19) and 1-benzal-2,3-diphenylhydrindene (20). Carbonation of the metallic addition compound produces 1-carboxy-2,3,4-triphenylnaphthalene (3). 1,4-Diphenyl-1,3-butadiyne,  $C_6H_5C \equiv C - C \equiv CC_6H_5$ , does not add lithium under corresponding conditions (3).

#### Addition to aromatic rings.

A further type of addition shown by lithium is that

18. Wittig and Waltnitzki, ibid., 67, 667 (1934).
19. Bergmann and Zwecker, Ann., 487, 155 (1931).
20. Bergmann and Schreiber, ibid., 500, 118 (1933).

involving the double bonds of aromatic rings and of rings attached to aromatic cycles. Such compounds as substituted anthracenes, indenenes, phenanthrenes, naphthalenes and even biphenyl show this ability to add lithium metal.

Anthracene itself, adds lithium metal slowly, for nine days in ether solution are necessary. Addition takes place at the 9- and 10- positions (3). The action of carbon dioxide gas on the addition product gives some 9,10-dihydro-9,10,10-tricarboxyanthracene (21). A superficial inspection might lead to the conclusion that three atoms of lithium added. This is probably not true, especially in view of some recent work which has been done on the carbonation of organoalkali compounds (22). This study shows that the manner of carbonation plays a large part in determining the products of carbonation. Thus the organosodium compound or compounds formed from n-amyl chloride and sodium give largely caproic acid with very little n-butylmalonic acid when carbonation is effected by solid carbon dioxide. A mixture of caproic acid with relatively large amounts of n-butylmalonic acid is formed when slow, gaseous carbonation is used to characterize the organometallic compound. These results indicate that the isolation of a compound with two carboxyl groups on a single carbon atom does not prove that

21. Blum-Bergmann, ibid., 484, 26 (1930).

22. Gilman and Pacevitz, J. Am. Chem. Soc., 62, 1301 (1940).



the precursory compound had two metal atoms on this same carbon.

9,10-Diphenylanthracene, when treated with lithium for two days in ether solution, adds two atoms of the metal. Carbonation of this addition product yields two 9,10-diphenyl-9,10-dicarboxyanthracenes which are stereoisomers (1). In a similar manner 9,10-dibenzylanthracene gives the corresponding 9,10-diacid (12). More highly substituted anthracenes like 1,2-dibenzanthracene (23), 1,2,3,4,5,6-tribenzanthracene, cholanthrene (24), and 3-methylcholanthrene (25) add lithium in ether solution. Hydrolysis of these addition compounds yields dihydro derivatives while carbonation introduces carboxylic acid groups. In some cases the exact positions entered are not known with certainty.

3-Phenylindene is reported to undergo dimerization when treated with lithium (21) but later workers have not been able to verify the reaction (26). 1,1,3-Triphenylindene, however, adds lithium and hydrolysis yields a dihydro compound which has not been positively identified (1). Benzalindene also adds lithium (27). When 1-biphenylene-3-phenylindene

23. W. E. Bachmann, J. Org. Chem., 1, 347 (1936).

24. W. E. Bachmann, ibid., 3, 434 (1938).

25. Bachmann and Pence, J. Am. Chem. Soc., 59, 2339 (1937).

26. Marvel and Pacevitz, ibid., 60, 2816 (1938).

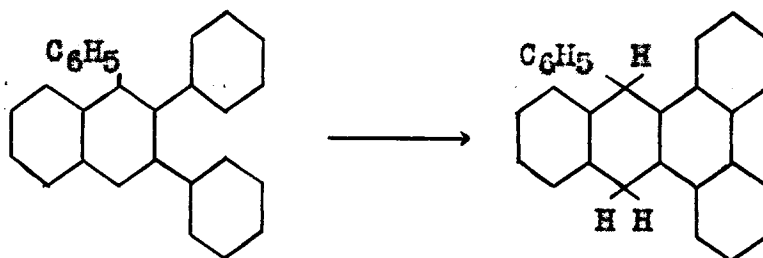
27. Ziegler and Schäfer, Ann., 511, 101 (1934).

is shaken with lithium in ether for three days and the resulting solution is then hydrolyzed, a fair yield of 1,2,3,4-dibenz-9-phenylfluorene is obtained (28).

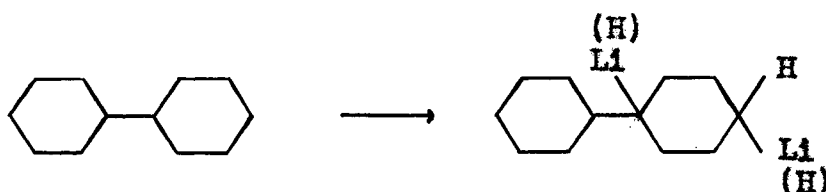
Phenanthrene adds lithium and hydrolysis produces a dihydrophenanthrene. Schlenk (3) thought this compound was the 1,4-dihydrophenanthrene because it could be further reduced by hydrogen with a catalyst. He assumed that the 9,10-dihydrophenanthrene could not be reduced in this manner. Schroeter (29), however, has shown that the reduction of phenanthrene takes place in three steps. This fact invalidates Schlenk's assumption. Adams (30) later showed that lithium, like the other alkali metals, adds to the 9,10-positions of phenanthrene. He used the dimethyl ether of ethylene glycol as solvent for the reaction because it has been shown that ethers of higher oxygen content than diethyl ether accelerate the addition of alkali metals to unsaturated linkages (31). Adams also showed that some of Schlenk's results were due to the presence of fluorene as an impurity in the phenanthrene used. The corresponding reaction of 9-phenylphenanthrene with lithium in ether forms a violet-colored solution, which is hydrolyzed to yield 9-phenyl-9,10-dihydrophenanthrene (32).

28. Koelsch and Rosenwald, J. Am. Chem. Soc., 59, 2170 (1937).
29. Schroeter, Müller and Huang, Ber., 62, 645 (1929).
30. Jeanes and Adams, J. Am. Chem. Soc., 59, 2608 (1937).
31. N. D. Scott, U.S. Patent 2,054,303 / C.A., 30, 7586 (1936)7.
32. Bergmann and Bergmann, J. Am. Chem. Soc., 59, 1443 (1937).

Naphthalene will add lithium in ether solution under similar conditions. Hydrolysis of the addition compound forms 1,4-dihydronaphthalene and carbonation produces 1,4-dicarboxy-1,4-dihydronaphthalene (1). 2,3,4-Triphenyl-naphthalene, one of the products formed by the action of lithium on diphenylacetylene (see page 19), also reacts with lithium (19). Hydrolysis, after shaking with lithium in ether for eight days, permits the isolation of 1,2,3,4-dibenz-9-phenyl-9,10-dihydroanthracene. This change involves ortho positions of two adjacent phenyl groups and resulting bond shifts, although in just what way this change takes place is not clear.



Biphenyl adds lithium very slowly. Hydrolysis of the reaction mixture after two weeks yields 1,4-dihydrobiphenyl and carbonation yields the 1,4-dicarboxylic acid (3).



Lycopin in ether forms a blue-green solution with lithium

which is hydrolyzed to one or more dihydrolycopins (33).

Pyrene adds lithium in ether solution. The product of carbonation is not definitely known but is probably 4,9- or 3,10-dicarboxy dihydropyrene (34).

#### Other reactions.

An interesting case of cleavage of a hydrocarbon is found in the reaction of 1,1,3,3,3-pentaphenyl-1-propene (1-triphenylmethyl-2,2-diphenylethylene) and lithium in ether. After several days, hydrolysis yields triphenylmethane and 1,1,4,4-tetraphenyl-2-butene. Carbonation of the reaction mixture produces triphenylacetic acid and 1,4-dicarboxy-1,1,4,4-tetraphenyl-2-butene (28). These products indicate that the hydrocarbon is cleaved to give two parts a triphenylmethyl radical and a 1,1-diphenylethenyl radical. The former adds lithium to form triphenylmethyllithium while the latter dimerizes, either before or after adding lithium, to form the substituted butene.

A similar case is reported in which dimerization occurs. 1-Bromo-2,2-diphenylethylene reacts with lithium in ether and hydrolysis of the resulting solution yields 1,1,4,4-tetraphenyl-2-butene. The action of iodine produces 1,1,4,4-

33. Karrer and Bachmann, Helv. Chim. Acta, **12**, 285 (1929).

34. Bergmann and Bograchov, J. Am. Chem. Soc., **62**, 3016 (1940).

tetraphenyl-1,3-butadiene (35). These results indicate that dimerization or coupling preceded addition of lithium.

Although many of the aromatic compounds add lithium metal, heterocyclic compounds like furan and 1-methylfuran are not affected by lithium (36).

### Preparation of Organolithium Compounds

#### Preparation by addition of lithium metal.

The preparation of organolithium compounds by addition of lithium metal to unsaturated molecules has been discussed above. This method is more or less limited because the types of molecules which will add lithium are rather few in number. Then, too, the compounds are complex and of a low order of reactivity as will be shown later.

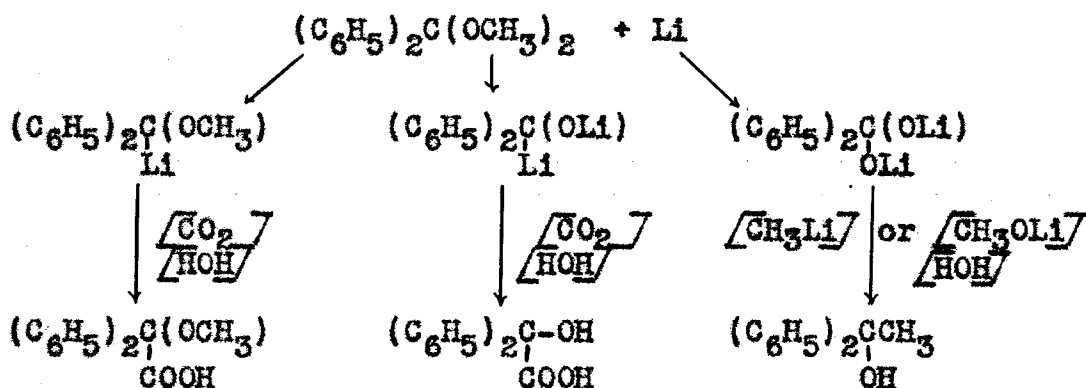
#### Preparation by ether cleavage.

Another method of preparation, which is still more limited, is that of cleaving ethers by lithium metal. Lithium is not a very powerful reagent for cleaving ethers. A few ethers are slowly cleaved by it. Diphenyldimethoxymethane, on shaking with lithium in ether for three weeks, forms a

35. Blum, Ber., 62, 881 (1929).

36. Gilman and Breuer, J. Am. Chem. Soc., 56, 1123 (1934).

red-violet colored solution. Hydrolysis yields diphenylmethylecarbinol and carbonation forms a small amount of diphenylmethoxyacetic acid and diphenylhydroxyacetic acid. These products are the results of side reactions following cleavage and are thought to be formed as shown in the following sequence of reactions (37):



Evidently cleavage takes place on either side of the oxygen atom.

In a similar manner 9,9-dimethoxyfluorene, 9-phenyl-9-methoxyfluorene and 9-phenyl-9-benzyloxyfluorene undergo slow cleavage by lithium in ether (1).

#### Preparation by metal displacement.

The simple alkyllithium compounds were first prepared by a reaction known as metal displacement. Schorigin, in 1910, had noted that diethylmercury and lithium in benzene gave some propionic acid on carbonation, but he did nothing

37. Schlenk and Bergmann, Ann., 464, 35 (1928).

further with the reaction (38). Schlenk and Holtz (39) were the first to carry out this reaction as a means of preparing the organolithium compounds, although the reaction had been used for many years to obtain the organosodium compounds. In fact Wanklyn had used it as early as 1858, reacting diethylzinc with sodium (40). Schlenk and Holtz treated organomercury compounds with lithium in solvents like gasoline or benzene and obtained good yields of the organolithium compounds. They used Schlenk tubes (41) filled with nitrogen. The reaction is slow and thorough shaking is necessary to obtain good yields. Heating increases the rate of reaction. Ziegler later showed that the reaction is reversible by shaking a solution of n-butyllithium in cyclohexane with a large excess of mercury (42). After two days no organolithium compound remained and the odor of di-n-butylmercury was very pronounced. Later he showed that benzyl lithium is converted almost completely into dibenzylmercury by shaking it for fifteen hours with excess mercury (43). The general reaction is written as follows:



In practice a large excess of lithium is used so that the

- 38. Schorigin, Ber., 43, 1938 (1910).
- 39. Schlenk and Holtz, ibid., 50, 262 (1917).
- 40. Wanklyn, Ann., 107, 125 (1858).
- 41. Schlenk and Thal, Ber., 46, 2843 (1913).
- 42. Ziegler and Colonius, Ann., 479, 135 (1930).
- 43. Ziegler, Ber., 64, 445 (1931).

reaction goes essentially to completion. The method is a convenient one in that it requires little attention but is rather expensive and also somewhat dangerous because it involves the use of the highly poisonous mercury compounds.

The method of Schlenk and Holtz was later improved by Marvel (44) who simplified the preparation by using solvent vapor as the inert atmosphere. Further extensions were made by Hein who prepared the simple alkyl lithium compounds from organozinc, -cadmium, and -aluminum compounds by this method (45). The reaction seems quite general. For example, bis 2-(5-ethylcarbazyl)mercury, when treated with lithium and then with carbon dioxide, yields fifty per cent of 2-carboxy-5-ethylcarbazole (46).

Ziegler and Dersch have effected metal displacement in Grignard reagents with lithium. Benzylmagnesium chloride and lithium in ether solution form benzyllithium, lithium chloride and magnesium (47). This preparation of benzyllithium is impractical, however, because a long time and dilute solutions are necessary for appreciable reaction to take place. Another recent extension of the method is that in which tetraphenyllead or triphenylbismuth are treated with lithium in ether or xylene (48). The yields of phenyl-

44. Hager and Marvel, J. Am. Chem. Soc., 48, 2689 (1926).
45. Hein, Petzchner, Wagler and Segitz, Z. anorg. allgem. Chem., 141, 161 (1924). [C.A., 19, 1080 (1925)]/.
46. Gilman and Kirby, J. Org. Chem., 1, 146 (1936).
47. Ziegler and Dersch, Ber., 64, 448 (1931).
48. Talalaeva and Kocheshkov, J. Gen. Chem. (U.S.S.R.), 8, 1831 (1938) [C.A., 33, 5819 (1939)]/.



lithium are poor and of no practical value. Other similar compounds, like tetraphenyltin, tetraphenylsilicon, triphenylarsine and diphenylmercury are reported to yield no phenyllithium under these conditions. These results are of no great value except they indicate that some conditions may be too drastic for this reaction. This is seen in the apparent failure of diphenylmercury to react, whereas the preparation of organolithium compounds from mercurials under milder conditions has been well established by the work of Schlenk and others as just mentioned.

Preparation by halogen replacement.

In general, the most satisfactory method of preparation of the simpler aliphatic and aromatic organolithium compounds is the direct replacement of a halogen atom by lithium. The first indications that this reaction would take place were obtained by Spencer and his coworkers. As early as 1908 a preliminary note reporting the reaction of  $\alpha$ -bromonaphthalene and lithium was published (49). The evidence was indirect, being based on the products isolated after hydrolysis. Among these was naphthalene in amount corresponding to forty per cent of the  $\alpha$ -bromonaphthalene used, indicating that  $\alpha$ -naphthyllithium had been formed. The statement was also made that they were unable to obtain any reaction in ether.

49. Spencer and Wallace, J. Chem. Soc., 1827 (1908).

Two years later the following general reactions were postulated (50):



These equations were based on the products isolated from hydrolyzed reaction mixtures of various organic halides and lithium which had been heated to reflux, without solvent, for periods of from three to twenty hours. Iodobenzene and lithium in ether were reported to form only biphenyl. Ziegler and Colonius (42) were unable to duplicate these results, but were successful in preparing the simple organolithium compounds in ether, benzene, cyclohexane and analogous solvents by reaction (I) (above). They used Schlenk tubes (41) in all their preparations. Gilman (51) later showed that Schlenk tubes are unnecessary and that the conventional Grignard apparatus can be employed.

The first reaction, (I), is, in general, most satisfactory with chlorides. The bromides or iodides are sometimes preferable as a matter of convenience. For example, methyl chloride gives a better yield of methyllithium than does the bromide or iodide. In small runs especially, the iodide is so much more convenient (because it is liquid at ordinary

50. Spencer and Price, *ibid.*, 385 (1910).

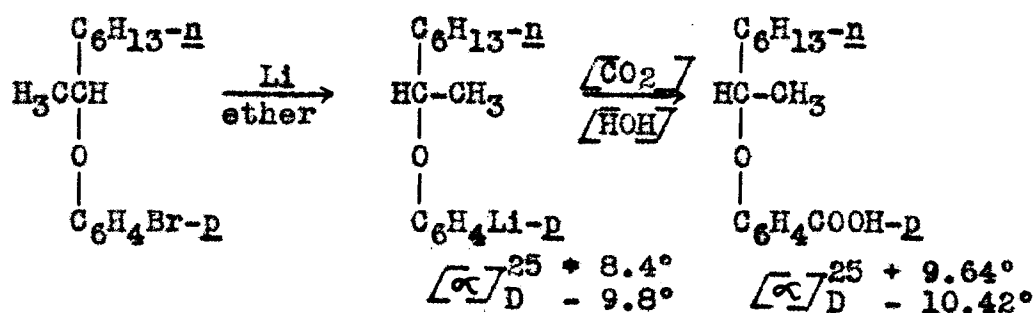
51. Gilman, Zoellner and Selby, *J. Am. Chem. Soc.*, **54**, 1957 (1932).

temperatures) that it is usually employed. Methyl iodide appears to be the exception in the aliphatic series for all the other iodides give very poor or no yields of organolithium compounds. Iodobenzene gives a fair yield of phenyllithium but bromobenzene is better and more economical. The reaction seems quite general in the aliphatic series for long-chained compounds like dodecyl- and tetradecyllithium have been prepared (52). Many less accessible organolithium compounds can be made by using special precautions. Such compounds as 3-styryllithium (53), 5-lithiotetralin (54), and 4-lithio-2,7-dimethylhydrindene (55) are obtainable from the bromides. Triphenylmethyllithium can be made from the chloride and five-tenths per cent lithium amalgam (56). Other halides, like 3-iodofuran (57), 2-bromofluorene, trifluorochloromethane (58) and 3-bromoacenaphthene (59), do not react with lithium under conditions tried thus far. 2-Bromo-3,4,6-triphenylpyridine and lithium in ether react, apparently to form 2-lithio-3,4,6-triphenylpyridine, for hydrolysis yields 2,4,5-triphenylpyridine (60). Strangely

52. Hoyt and Gilman, Proc. Iowa Acad. Sci., 45, 133 (1938).
53. Wright, J. Org. Chem., 1, 457 (1936).
54. Cook and Lawrence, J. Chem. Soc., 1431 (1936).
55. Bruce, J. Am. Chem. Soc., 60, 2277 (1938).
56. v. Grosse, Ber., 59, 2646 (1926).
57. Gilman and Wright, J. Am. Chem. Soc., 55, 2893 (1933).
58. Simons, Bond and McArthur, ibid., 62, 3477 (1940).
59. Miller and Bachman, ibid., 57, 766 (1935).
60. Allen and Frame, ibid., 62, 1301 (1940).

enough, this lithium compound did not react with carbon dioxide, aldehydes or ketones.

In the formation of organolithium compounds from optically active halides, racemization occurs if the halogen is on the asymmetric carbon atom (61). The unreacted halide is not racemized during the reaction. If the asymmetric center is not the point of reaction then racemization does not take place (62).



Organolithium compounds, therefore, may be used to introduce optically active groups into molecules. (See page 82 for such a reaction).

The rates of formation of organolithium compounds in ether are more rapid than those of the corresponding Grignard reagents. They follow, in general, the reactivities of the halogens and the aliphatic halides are more reactive than the corresponding aromatic compounds (63).

61. Tarbell and Weiss, *ibid.*, 61, 1203 (1939).
62. Austin, *ibid.*, 55, 2948 (1933).
63. Gilman, Zoellner, Dickey and Selby, *ibid.*, 57, 1061 (1935).

The yields of organolithium compounds are dependent on several factors such as solvent (42), rate of addition of halide and fineness of the metallic lithium (64, 65, 66). The more finely divided lithium metal is generally better. Various ways of obtaining finely divided lithium have been devised (67).

The advantages of using low-boiling petroleum ether as a solvent for the preparation of the lower alkyllithium compounds (except methyllithium) have only recently received the recognition they deserve (67). The rates of formation of alkyllithium compounds in this solvent approach those in ether and higher yields are obtained. The difficulty of secondary reactions like cleavage, present in diethyl ether, is obviated. Indirect supplementary analyses (68) are unnecessary to determine the titer of solution, and the simple acid-titration analysis (69) is adequate. The by-product of the reaction, lithium halide, as well as other inorganic lithium compounds such as the oxide and nitride, are insoluble in petroleum ether and are removed by filtration (67). The production of such compounds as isopropyl- and s-butyllithium

64. Gilman, Zoellner and Selby, ibid., 55, 1252 (1933).
65. Gilman, Zoellner, Selby and Boatner, Rec. trav. chim., 54, 584 (1935).
66. Morton and Hechenbleikner, J. Am. Chem. Soc., 58, 1697 (1936).
67. Gilman, Langham and Moore, ibid., 62, 2327 (1940).
68. Ziegler, Crössmann, Kleiner and Schäfer, Ann., 473, 1 (1929).
69. Gilman, Wilkinson, Fishel and Meyers, J. Am. Chem. Soc., 45, 150 (1923).

is much more satisfactory. t-Butyllithium has been synthesized for the first time, using this solvent (see page 89). The low boiling point of the solvent facilitates its removal and replacement by other solvents.

#### Preparation by interconversion.

Three general types of interconversion reactions are recognized at present in organometallic chemistry. These are: hydrogen-metal interconversion or metalation, halogen-metal interconversion and metal-metal interconversion. All of these types of reaction may be used to prepare organolithium compounds. Since they are more or less supplementary to the more direct methods no discussion of them will be made at this point but will be deferred to allow a complete treatment of the three types to be made in the next section (see pages 57 to 76 inclusive).

### Properties of Organolithium Compounds

#### Physical properties.

The organolithium compounds have not been extensively examined in regard to their physical and physico-chemical properties. With few exceptions most of the reported data of this nature have been recorded incidentally to the study of some chemical reactions.

The lower alkylolithium compounds, so far as has been determined, are liquids with the exception of methyl- and ethyllithium which are fusible solids (39). Fusion does not decompose these compounds but prolonged heating in solvents at temperatures above their melting points slowly breaks them down. Thus, ethyllithium, after heating in ligroin for several hours at 120°, gave, on hydrolysis, hydrogen gas corresponding to fifty per cent decomposition (4).



Hein and coworkers have studied the electrical conductivities of various organolithium compounds in several solvents (45). Their results may be briefly summarized as follows: Methyl-, ethyl-, phenyl- and benzylolithium all conduct in diethylzinc. Ethyllithium, fused or in benzene solution, does not conduct. The molar conductance of a solution of ethyllithium in diethylzinc decreases with increased dilution indicating increased solvation. In diethylzinc solution, methylolithium is a better conductor than ethyllithium. Ethyllithium conducts better in triethylaluminum solution than in diethylzinc solution, but is a non-conductor in diethylcadmium. Phenylolithium is a poor conductor in diethylzinc while benzylolithium is the best conductor of all the alkylolithium compounds studied. From

cryoscopic data Hein showed that ethyllithium is associated into aggregates of six or seven molecules in benzene solution while the solvates with diethylzinc are represented by  $\sqrt{C_2H_5Li \cdot (C_2H_5)_2Zn}_2$  and larger aggregates (70). In ether solution most of the organolithium compounds apparently associate with the solvent. These etherates sometimes separate from solution on long standing (56, 71). A general comparison of the physical properties of the alkyl derivatives of the elements, including those of lithium, with respect to their positions in the Periodic System has been made (72).

#### Chemical properties.

Organolithium compounds are of interest chiefly because of their chemical properties. In a broad sense they react in various ways which may be classified as follows: They add to multiple linkages in many types of compounds. They take part in many interconversions and other cleavage reactions. They enter into many coupling reactions. They react with salts and also give various other reactions of less importance. Due to the high reactivities of these compounds towards carbon dioxide, moisture and oxygen the organolithium compounds

- 70. Hein and Schramm, Z. physik. Chem., 151A, 234 (1930).
- 71. Ziegler and Schäfer, Ann., 479, 150 (1930).
- 72. v. Grosse, Z. anorg. allgem. Chem., 152, 133 (1926).



must be prepared and manipulated in an inert atmosphere free of these substances. Nitrogen is usually used although other gases like methane, butane, hydrogen or even helium might be used. The use of hydrogen is discouraged because of the ease with which air-hydrogen mixtures are exploded.

Addition to multiple bonds. One of the multiple linkages to which organolithium compounds add is the carbon-carbon double bond. The simplest case is that of ethylene, which is polymerized to non-gaseous products by the lower alkylolithium compounds (73). Ziegler and his coworkers have done most of the work on this reaction. Unsymmetrical diphenylethylene (isostilbene) adds *n*-butyllithium slowly in benzene solution. After fourteen days at room temperature, carbonation yields fifty per cent of 2,2-diphenylheptanoic acid (68). sym. Diphenylethylene yields the corresponding 2,3-diphenylheptanoic acid under similar conditions. Other organolithium compounds also add to these compounds. 1,3-Butadiene has been made the subject of rather intensive study as regards its polymerization by organoalkali compounds. In general, lithium compounds of the types (aryl)<sub>2</sub> α(H)CLi and (aryl)<sub>3</sub>CLi cause it to polymerize. Among the compounds studied were those of fluorene, indene, phenylindene and 1,3-diphenylindene (74). With benzyllithium in ether, butadiene

73. Friedrich and Marvel, J. Am. Chem. Soc., 52, 376 (1930).  
74. Ziegler and Jakob, Ann., 511, 45 (1934).

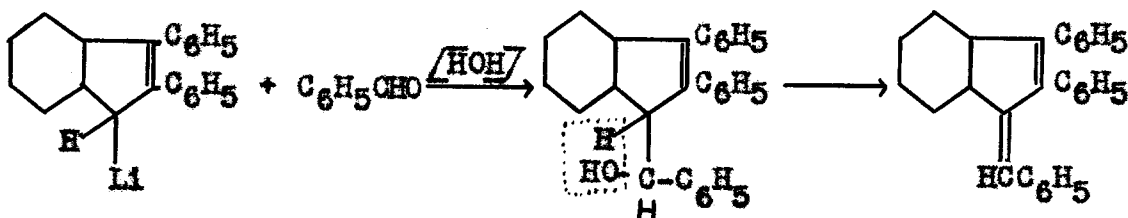
yields, subsequent to hydrogenation, phenylated hydrocarbons like phenylnonane and phenyltridecane (75). Some of the most recent work has been done with n-butyllithium. With this compound in ether at 25-30°, butadiene yields, after hydrolysis, nine to thirty-one per cent octenes and eighteen to thirty-four per cent dodecadienes in addition to some high-boiling products. In benzene solution at 100-115° the products isolated seem largely the result of 1,4-addition while in ether at -50°, 1,2-addition is the main reaction (76). Temperature apparently plays a dominant role in the addition reaction, for if seven moles of butadiene and one mole of n-butyllithium are reacted at 150° and the product is then ozonized and hydrolyzed, a sixty per cent yield of succinic acid is obtained. The same reaction, run at -80°, produces no succinic acid. Strangely enough, 1,1,5,5-tetraphenyl-1,4-pentadiene does not add phenyllithium but is metalated by it (77). The organolithium compound formed exists in two allylic forms similar to those previously described (see page 13).

Dimethylfulvene and dimethylbenzofulvene add phenyllithium in ether solution but hydrolysis produces only resinous materials from which no starting compounds can be isolated (27).

75. Ziegler, Dersch and Wollthan, ibid., 511, 13 (1934).  
76. Ziegler, Grimm and Willer, ibid., 542, 90 (1939).  
77. Wittig and Obermann, Ber., 68, 2214 (1935).

The carbonyl group,  $>C=O$ , is another important multiple linkage acted upon by organolithium compounds. The reactions of the common aldehydes and ketones with organolithium compounds have not been extensively studied. Usually, for the purpose of synthesis, the Grignard reagent is employed, largely because the reactions have been well established and the reagent is readily available. Some more complex ketones have been reacted with organolithium compounds, however, and in certain cases the use of the latter reagents makes possible the syntheses of molecules which cannot be made by the use of the Grignard reagent.

With benzaldehyde the action of organolithium compounds is 1,2-addition to the carbonyl group. Thus the lithium compound formed from 9-allylphenanthrene (see page 17) reacts with benzaldehyde to form 1-phenyl-2-(9-phenanthryl)-3-buten-1-ol in fair yield (9). 1-Lithio-2,3-diphenylindene and benzaldehyde yield 1-benzal-2,3-diphenylindene, which is the dehydration product of the carbinol first formed (19).

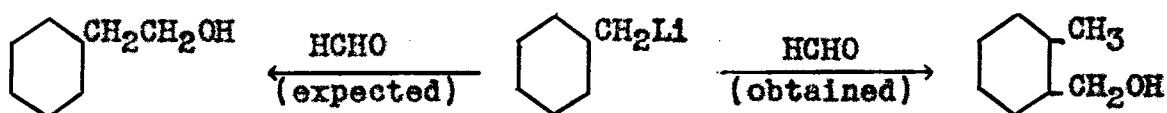


The compound formed by metalating 3,5-diethyl-2-*n*-propylpyridine reacts with benzaldehyde and with butyric aldehyde to

give the 2-( $\alpha$ -benzyloxy) and 2-( $\alpha$ -butanoxy) derivatives, respectively (78).



Benzyllithium, like benzylmagnesium chloride, reacts with formaldehyde to give *o*-tolylcarbinol instead of the expected  $\beta$ -phenylethyl alcohol (6). This is another case of allylic rearrangement. An explanation of this reaction from the standpoint of quantum mechanics has been proposed (79). Such vigorous protests have been made against this



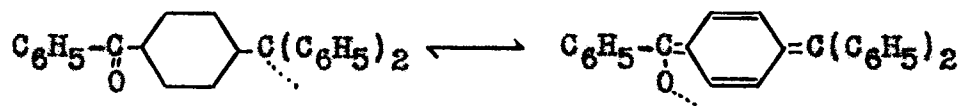
proposal, however, that it is of doubtful value (80, 81).

Benzophenone reacts with organolithium compounds to form carbinols. For example, 9-fluorenyllithium yields 9-fluorenyldiphenylcarbinol with benzophenone in ether solution (1). Other organolithium compounds which react with this ketone in the same manner are *o*-anisyllithium (82),

78. Haskelberg, Chemistry and Industry, 54, 261 (1935).
79. Nilsen, J. Chem. Physics, 3, 15 (1935).
80. Hylleraas, ibid., 3, 313 (1935).
81. Pauling and Wheland, ibid., 3, 315 (1935).
82. Wittig, Pockels and Dröge, Ber., 71, 1903 (1938).

p-anisyllithium (83), 2,5-dimethoxyphenyllithium, 2,4-dimethoxyphenyllithium, 5-bromo-2,4-dimethoxyphenyllithium (82), and 3-styryllithium (84). With 1-lithio-3-phenylindene (21) benzophenone reacts to give an unsaturated derivative in a manner similar to that shown with 2,3-diphenylindenyllithium and benzaldehyde (see page 39). 1-Lithio-8-methylnaphthalene reacts with o-chloroacetophenone in an analogous manner (85).

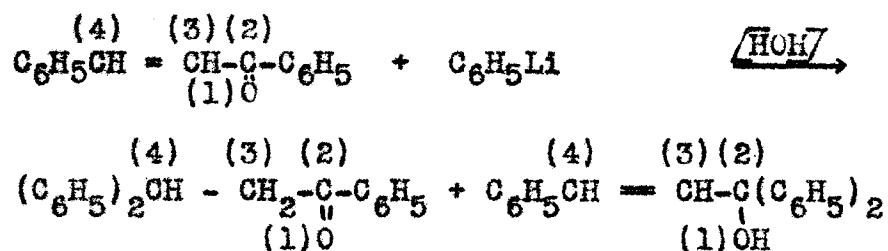
Substituted benzophenones also react with organolithium compounds. The product obtained is dependent upon the nature of the substituent groups. Thus, bis (4-benzylphenyl) ketone and phenyllithium react normally to give bis (4-benzylphenyl) phenylcarbinol in almost quantitative yield (86). Although 4-benzohydrylphenyl phenyl ketone reacts normally with phenyllithium, the related compound 4-( $\alpha$ -chlorobenzohydrylphenyl) phenyl ketone does not undergo addition but reacts to form a free radical which apparently exists in two forms, one having a trivalent carbon atom, the other a monovalent oxygen atom (87). These forms are as follows:



83. Müller and Töpel, ibid., 72, 273 (1939).
84. Marvel, Mueller and Peppel, J. Am. Chem. Soc., 60, 410 (1938).
85. Fieser and Seligman, ibid., 61, 136 (1939).
86. Connerade, Bull. soc. chim. Belg., 45, 647 (1936).
87. Wittig, Kairies and Hopf, Ber., 65, 767 (1932).

The reaction of phenyllithium with bis (4-dichloromethyl-phenyl) ketone gave only polymeric products (88).

In contrast to the Grignard reagent, the reaction of organolithium compounds with most conjugated systems containing a carbonyl group is nearly always 1,2-addition to the carbonyl group. Although the Grignard reagent reacts in this manner with some conjugated systems, such as is found in benzophenone, other more active systems do not always yield the same product with this reagent and with the corresponding organolithium compound. For example, benzalacetophenone reacts with phenyllithium to give about ninety per cent of diphenyl-β-styrylcarbinol, the 1,2-addition compound (89) and about ten per cent of the 1,4-addition product, β,β-diphenylpropiophenone (90).

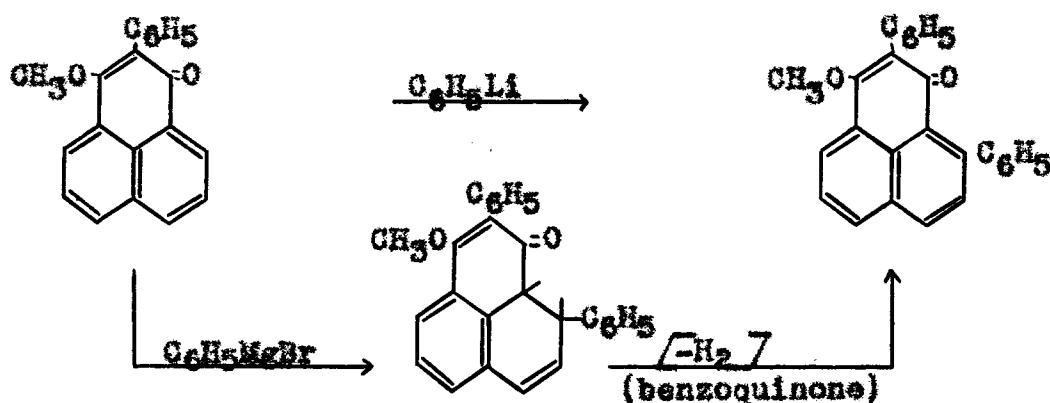


The ratio of products is approximately the same with p-dimethylaminophenyllithium (90). Under somewhat different conditions Wittig has isolated 1,1,3,5,5-pentaphenyl-1,5-dioxypentane as the major product (91).

88. Connerade, Bull. soc. chim. Belg., 43, 447 (1934).
89. Lüttringhaus, Ber., 67, 1602 (1934).
90. Kirby, Iowa State Coll. J. Sci., 12, 137 (1937).
91. Wittig and Kosack, Ann., 529, 167 (1937).

With dibenzalacetone,  $\beta$ -styryllithium gives a fair yield of tri- $\beta$ -styrylcarbinol, the result of 1,2-addition to the carbonyl group (84).

A case where an organolithium compound gives a better yield of 1,4-addition product than the corresponding Grignard reagent is that in which 9-methoxy-8-phenyl-peri-naphthindan-7-one is reacted with phenyllithium and with phenylmagnesium bromide (92).

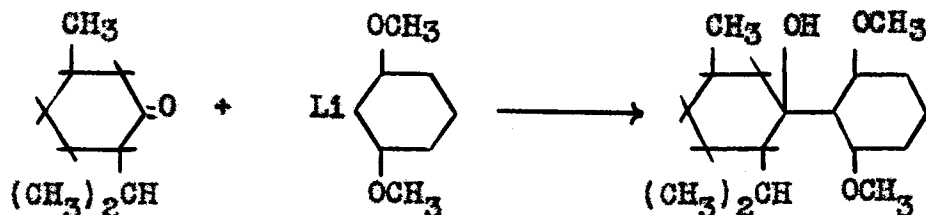


The yield with phenyllithium was twenty per cent and very poor with the phenylmagnesium bromide. The removal of hydrogen from the intermediate compound will be discussed later (see page 84). In the reaction of phenyllithium with the related 8-phenyl-peri-naphthindan-7,9-dione this same 1,4-addition took place but the dehydrogenation did not (92).

Other cyclic ketones have been reacted with organolithium compounds. Adams and coworkers have recently used

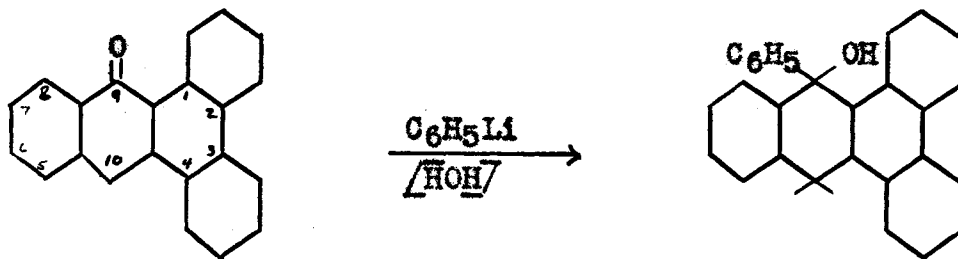
92. Koelsch and Rosenwald, J. Am. Chem. Soc., 59, 2166 (1937).

this combination in elucidating the structure of cannabidiol. For example, 3-methyl-6-iso-propylhexanone and 2,6-dimethoxyphenyllithium react to form 1-(2,6-dimethoxyphenyl)-3-methyl-6-iso-propylhexan-1-ol (93).



Other similar syntheses have been carried out (94).

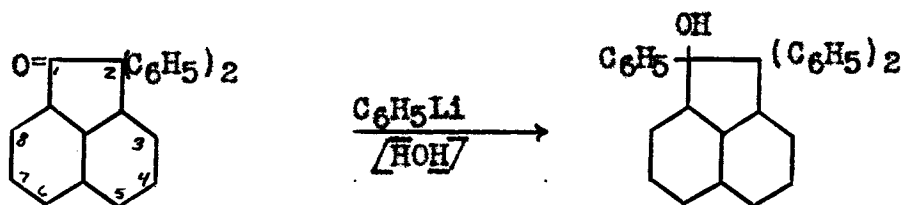
When 1,2,3,4-dibenz-9-anthrone is treated with phenyllithium and the addition product is hydrolyzed, 9-hydroxy-9-phenyl-9,10-dihydro-1,2,3,4-dibenzanthracene is obtained (95).



With 2,2-diphenyl-1-acenaphthenone, phenyllithium yields 1-hydroxy-1,2,2-triphenylacenaphthene (96).

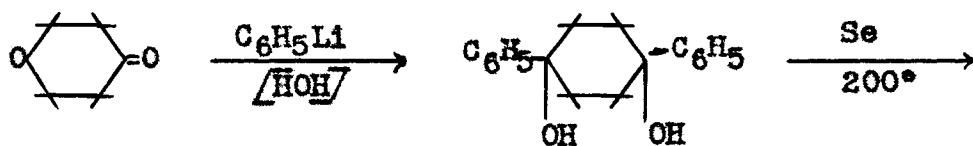
93. Adams, Wolff, Cain and Clark, *ibid.*, **62**, 1770 (1940).
94. Adams, Wolff, Cain and Clark, *ibid.*, **62**, 2215 (1940).
95. Bergmann and Berlin, *J. Chem. Soc.*, 493 (1939).
96. Wittig and Petri, *Ber.*, **68**, 924 (1935).



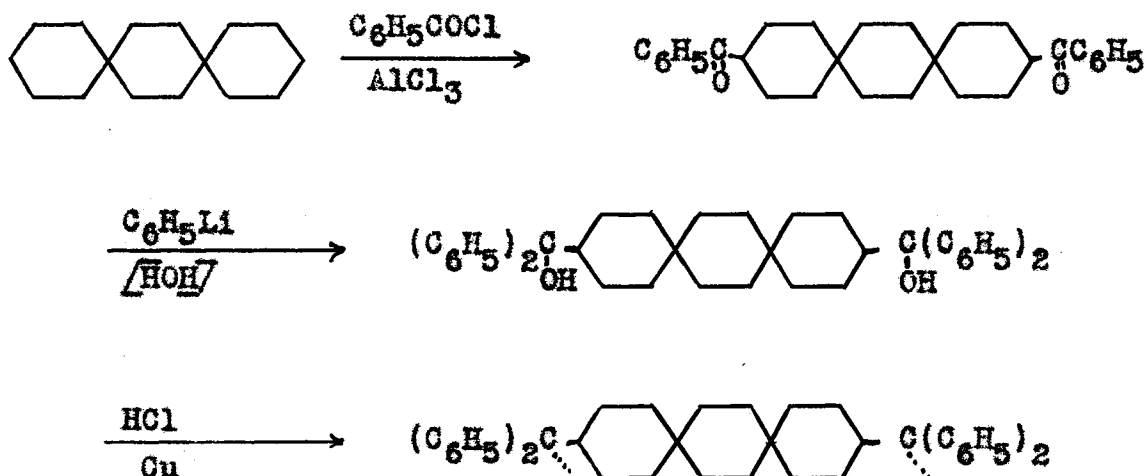


Methyl lithium has been used in a synthesis of a highly substituted anthracene derivative (97). The yield was very poor.

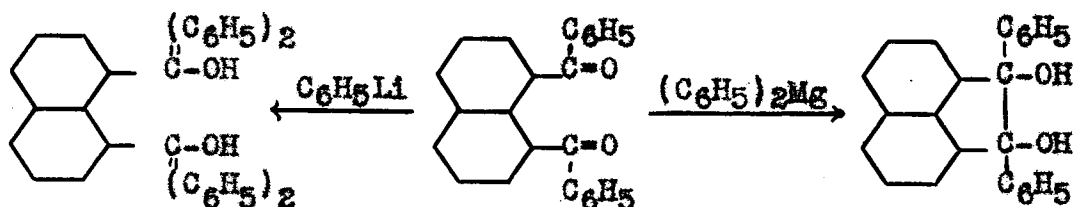
Compounds containing more than one carbonyl group also add organolithium compounds, usually undergoing 1,2-addition to this group. 1,4-Cyclohexandione and phenyllithium in ether give 1,4-diphenyl-1,4-cyclohexandiol in sixty per cent yield. This compound can be converted into terphenyl by heating at 200° with selenium. A Friedel-Crafts reaction with the terphenyl and benzoyl chloride yields 1,4-di-(4-benzoylphenyl)-benzene. The action of phenyllithium on this dicarbonyl compound produces a di-alcohol. Treatment with hydrogen chloride followed by copper metal produces a radical having two tri-valent carbon atoms (98). This sequence of reactions is illustrated by the following equations.



97. Fieser and Cason, *J. Am. Chem. Soc.*, 62, 432 (1940).  
 98. Müller and Sok, *Ber.*, 70, 1990 (1937).



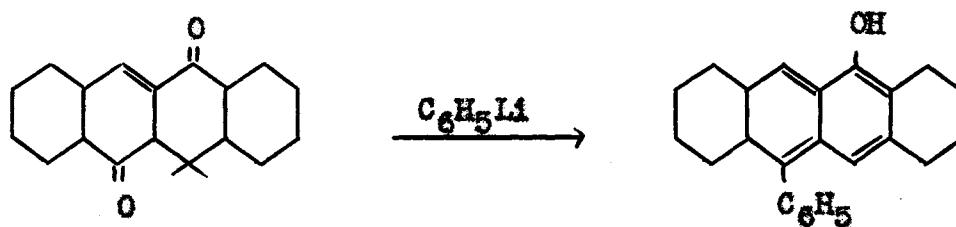
With derivatives of naphthalic acids the action of organolithium compounds is again unlike that of the corresponding Grignard reagent. In these cases the lithium compound gives 1,2-addition to the carbonyl group while the magnesium compound shows a reducing action. Thus, with 1,8-dibenzoylnaphthalene, phenyllithium adds 1,2- to the two carbonyl groups and the magnesium compound gives a ring closure (99).



The reaction of bis (4-benzoylphenyl) ketone with phenyllithium takes place smoothly to give good yields of 99. Wittig, Leo and Wiemer, *ibid.*, 64, 2405 (1931).

the expected bis( $\alpha$ -hydroxy- $\alpha$ , $\alpha$ -diphenyl-p-tolyl)phenylmethanol (100). Phenyllithium also reacts with bis 2,2'-(1-phenylinden-3-one) to give bis 2,2'-(1,3-diphenylinden-3-ol) in seventy per cent yield (101).

The following reactions were carried out in a study of the cyclization of benzylidenebenzylsuccinic acid (102). Methyl benzylsuccinate was treated with benzaldehyde and the mixture was distilled to yield a compound  $C_{18}H_{14}O_3$ , which was thought to be 2-benzyl-3-carboxy-1-hydroxynaphthalene or some isomer of this compound. This was treated with glacial acetic acid giving benzylidenebenzylsuccinic acid which was treated with sulfuric acid at  $70^\circ$  to form a compound  $C_{18}H_{12}O_2$ . This compound was treated with a large excess of phenyllithium to give a compound  $C_{24}H_{16}O$ , which was thought to be 1-hydroxy-10-phenyl-2,3-benzanthracene. The reaction involving the organolithium compound is shown below.



The reaction is described in the words of Bergmann (102):

100. Connerade, Bull. soc. chim. Belg., 46, 179 (1937).
101. Eck and Marvel, J. Am. Chem. Soc., 57, 1898 (1935).
102. Bergmann and Weizmann, Compt. rend., 209, 539 (1939).

"Evidently the phenyllithium reacts on the saturated ketonic group, enolizing the other ketonic group simultaneously and creating an entirely aromatic molecule."

Quinones react in the normal manner with organolithium compounds. Naphthoquinones (103), naphthacene quinones (104) and anthraquinones (105) have been reacted with phenyllithium.

1,1-Diphenyl-2-benzoyl-ethyl alcohol and phenyllithium react at  $-80^{\circ}$  to form 1,1,3,3-tetraphenylpropan-1,3-diol by 1,2-addition (2).

An interesting and useful application of the addition of relatively reactive organometallic compounds to the carbonyl group of Michler's ketone has been made as the basis of a color test for the qualitative determination of these compounds (106). Organolithium compounds give a positive test readily. This indicates that these compounds do not form stable addition complexes with Michler's ketone as do many less reactive organometallic compounds (107).

Some  $\alpha$ -oxido ketones and phenyllithium react to give good yields of the corresponding propanols. The first reaction is one of addition. Thus, with benzal-*p*-methoxy-acetophenone oxide and phenyllithium at  $-15^{\circ}$  in ether, the

- 103. Crawford, J. Am. Chem. Soc., 61, 3310 (1939).
- 104. Bergmann, J. Chem. Soc., 1147 (1938).
- 105. Weizmann, Bergmann and Haskelberg, ibid., 391 (1939).
- 106. Gilman and Schulze, J. Am. Chem. Soc., 47, 2002 (1925).
- 107. Gilman and Jones, ibid., 62, 1243 (1940).

following reaction occurs.



At reflux temperature cleavage of the oxide ring takes place giving diphenyl-*p*-anisylcarbinol and a resinous material (108). In a similar manner analogous reactions are obtained with *q*-chlorobenzalacetophenone oxide and other  $\alpha$ -oxido ketones (108, 109). These results are somewhat different from those obtained with Grignard reagents (110).

The usual reaction of the more active organometallic compounds with carbon dioxide is the formation of the salt of a carboxylic acid. It has been shown, however, that the common procedure of gaseous carbonation leads to very little acid from many organolithium compounds but that the chief product is a ketone, some tertiary carbinol also being formed. To overcome this difficulty, carbonation by slow addition to a large excess of crushed solid carbon dioxide is recommended (111). These secondary reactions leading to ketones and carbinols seem to be partially due to the solubility of the  $\text{RCOOLi}$  compound in ether, the usual solvent, because the other organoalkali compounds, whose salts are largely insoluble in ether, give high yields of acids (as salt) when

108. Bickel, *ibid.*, 59, 325 (1937).

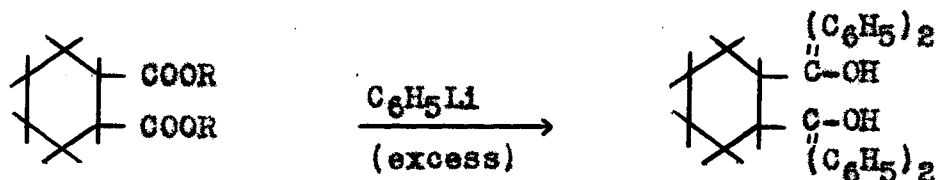
109. Kohler and Bickel, *ibid.*, 57, 1099 (1935).

110. Bergmann and Wolff, *ibid.*, 54, 1644 (1932).

111. Gilman and Van Ess, *ibid.*, 55, 1258 (1933).

carbonated in boiling ether solution (112).

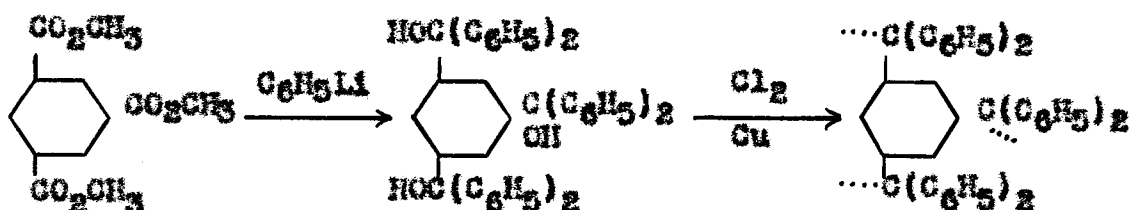
In general, the reaction of esters of carboxylic acids with excess organolithium compounds leads to tertiary carbinols. A great many esters have been so reacted. Dimethyl  $\alpha,\alpha'$ -dihydromuconate and excess phenyllithium yield 1,1,6,6-tetraphenyl-3-hexen-1,6-diol (11), while dimethyl meso-3,3'-diphenyladipate yields 1,1,3,4,6,6-hexaphenylhexan-1,6-diol (84). Methane triacetic acid trimethyl ester, under similar conditions, is converted to tri (3,3-diphenyl-3-oxyethyl)methane (91). The reaction is similar with esters of aromatic acids. Methyl 8-benzohydryl-1-naphthoate forms diphenyl-1-(3-benzohydrylnaphthyl)carbinol (96). Wittig has shown the following reaction to be quite general (18):



Cis and trans forms do not undergo stereoisomeric rearrangement during the reaction. The corresponding 1,4-diesters react in an analogous manner (113). Other organolithium compounds, like p-biphenyllithium (114), may also be used. With esters of aromatic dicarboxylic acids, the reaction is very good and yields as high as ninety per cent and more are

112. Gilman and Young, J. Org. Chem., 1, 315 (1936).  
 113. Wittig and Pook, Ber., 70, 2485 (1937).  
 114. Wittig and Kröhne, Ann., 529, 142 (1937).

obtainable (115). Leo has used this reaction to prepare a radical having three trivalent carbons (116). The sequence of reactions follows:

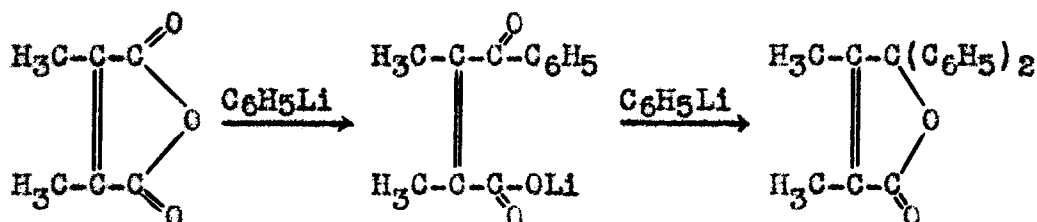


Other esters have also been reacted with phenyllithium (2, 117).

9-Fluorenyllithium reacts with dimethyl carbonate to form methyl fluorene-1-carboxylate in fair yield (21) and with ethyl orthoformate to yield an amorphous polymer (59). 1-Lithio-3-phenylindene and dimethyl carbonate react, yielding methyl 2-phenylindene-1-carboxylate (118).

Organolithium compounds react with acid anhydrides. The action of two moles of phenyllithium on one mole of dimethylmaleic anhydride gives 2,3-dimethyl-4,4-diphenylcrotonolactone which probably results from 1,2-addition of a second mole of organometallic compound to the intermediate keto acid formed (119).

- 115. Wittig and Leo, Ber., 64, 2395 (1931).
- 116. Leo, ibid., 70, 1691 (1937).
- 117. Wittig and Petri, Ann., 505, 17 (1933).
- 118. Blum-Bergmann, ibid., 492, 277 (1932).
- 119. Tarbell and Weaver, J. Am. Chem. Soc., 62, 2747 (1940).



This mechanism is substantiated by the action of phenyllithium on the intermediate keto acid,  $\beta$ -benzoyltiglic acid, to form the same lactone as was obtained in the above reaction. Only a small amount of material resulting from 1,4-addition was obtained. With phenylmagnesium bromide the same intermediate compound is obtained (120) but the excess Grignard reagent adds 1,4- to this compound instead of 1,2- as does the phenyllithium.

With phthalic anhydride the reaction is vigorous but not well defined. One of the products formed is triphenylcarbinol (115).

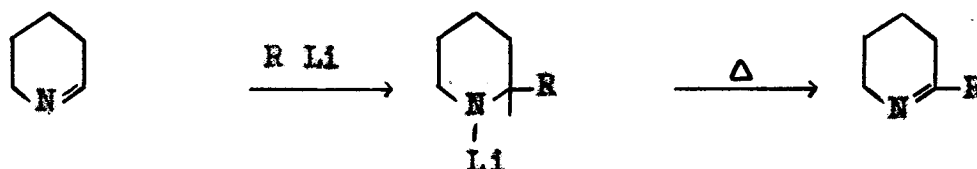
Organolithium compounds add to the carbon-nitrogen double bonding known as the anil linkage. This reaction was first reported by Ziegler and Zieser. They treated pyridine with benzene solutions of *n*-butyl- and phenyllithium finally heating the mixtures in sealed tubes at 90-100° for several hours (121). The first reaction is addition of the organolithium compound to the anil linkage to form an  $\alpha$ -substituted

120. Tarbell, *ibid.*, 60, 215 (1938).

121. Ziegler and Zeiser, *Ber.*, 63, 1847 (1930).



N-lithiodihydropyridine. Hydrolysis yields the  $\alpha$ -substituted dihydropyridine. On heating the unhydrolyzed addition compound, lithium hydride splits out leaving an  $\alpha$ -substituted pyridine. This sequence of reactions is shown below.

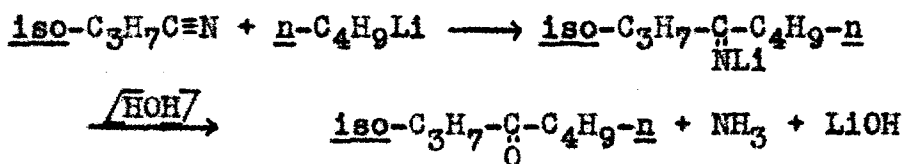


The yield of substituted pyridine was increased by replacing benzene, the solvent first used, by toluene (122). The extension of this reaction to other nitrogen compounds facilitated the preparation of many otherwise difficultly accessible products. Some of the compounds which have been reacted with organolithium compounds in this manner are acridine, which forms 9,10-dihydro-9-R-acridines, isoquinoline, 9,10-dihydro-acridine, which gives 9,10-dihydro-10-R-acridines (123), quinoline, 2-n-butylpyridine and quinaldine (124). This reaction has been used recently to prepare some substituted quinolines for possible use as insecticides (125).

The reaction of the nitrile group,  $-C\equiv N$ , with organolithium compounds is analogous to that of the Grignard reagent.

122. Walters and McElvain, J. Am. Chem. Soc., 55, 4625 (1933).
123. Bergmann, Blum-Bergmann and v. Christiani, Ann., 483, 80 (1930).
124. Ziegler and Zeiser, ibid., 485, 174 (1931).
125. Oldham and Johns, J. Am. Chem. Soc., 61, 3289 (1939).

The addition product is a ketimine which hydrolyzes more or less readily, to form a ketone. Thus, isobutyronitrile and n-butyllithium yield n-butyl iso-propyl ketone (126).

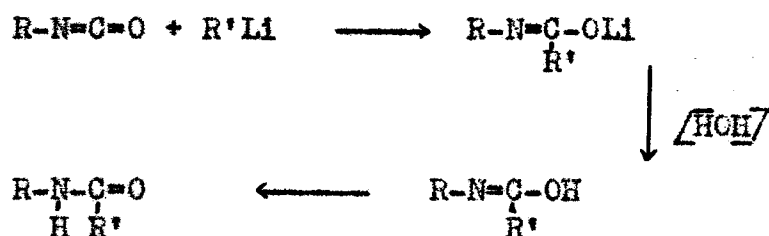


Some nitriles, which react only very slowly with Grignard reagents under the usual conditions, undergo prompt reaction with organolithium compounds (127, 128). For example, p-dimethylaminobenzonitrile and p-methoxybenzonitrile react smoothly with methyl- and phenyllithium to give the expected ketones, following hydrolysis. Other nitriles, which have been reacted with organolithium compounds, include benzonitrile and o-toluonitrile (112, 127, 128, 129). These have been studied mainly in determinations of the relative reactivities of various organometallic compounds. 1-Lithio-8-methylnaphthalene reacts with 4-cyanohydrindene to give the ketimine which could not be hydrolyzed to the ketone (130).

Compounds containing an anil linkage and some other functional group capable of reacting with organolithium compounds

- 126. Ziegler and Ohlinger, Ann., 495, 84 (1932).
- 127. Gilman and Kirby, J. Am. Chem. Soc., 55, 1265 (1933).
- 128. Gilman and Lichtenwaller, Rec. trav. chim., 55, 561 (1936).
- 129. Gilman, Kirby, Lichtenwaller and Young, ibid., 55, 79 (1936).
- 130. Fieser and Bowen, J. Am. Chem. Soc., 62, 2103 (1940).

have been studied, also. Thus, a compound with a coupled anil linkage and carbonyl (or thiocarbonyl) group is known to undergo 1,2-addition to the carbonyl group, although the end product obtained indicates that addition takes place at the anil linkage. For example, phenyl isothiocyanate has been shown to react in this way (131). This general reaction may be illustrated as follows:

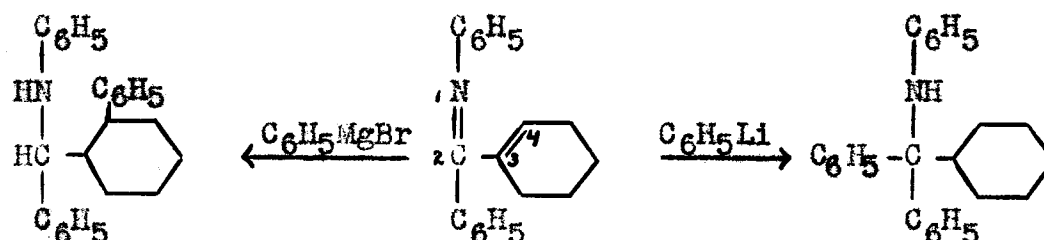


Acridone and 3-methylacridone undergo 1,2-addition at the carbonyl group (132). The anil linkage also takes part in the reaction for, if the N-potassium salt is used, only one-half the amount of phenyllithium necessary to react with the free base is needed to give equivalent reaction with the salt.

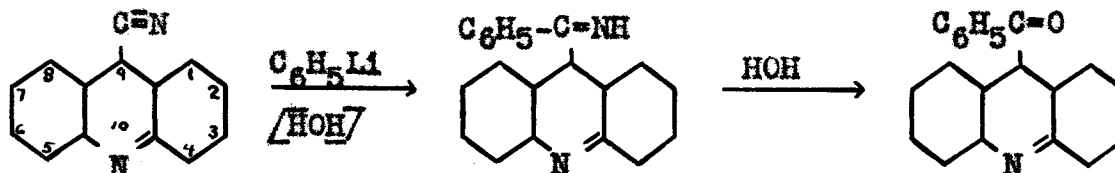
Benzophenone anil also adds phenyllithium. Here 1,2-addition to the anil linkage takes place, to form triphenylmethylaniline. The Grignard reagent adds 1,4- to the conjugated system (127). These two reactions are given below.

131. Gilman and Breuer, ibid., 55, 1262 (1933).

132. Lehmstedt and Dostal, Ber., 72, 804 (1939).



With 9-cyanoacridine, reaction takes place at the nitrile group. Using phenyllithium, the products isolated are 9-benzoylacridine and phenyl-(9-acridyl)iminomethane. The latter compound is unhydrolyzed ketimine (132).

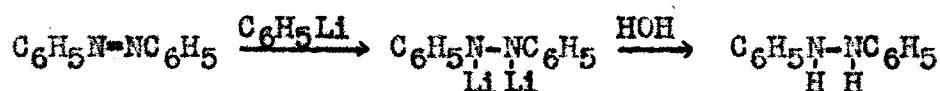


The anil linkage apparently does not play an important part in this reaction. 8-Cyanoquinoline reacts with 4-lithio-7-methylhydrindene to give the corresponding ketone in fifty-seven per cent yield (133). The 5-cyano compound gave a much poorer yield, seventeen and one-half per cent.

The nitrogen-nitrogen double bonding also reacts with organolithium compounds. Two reactions seem to take place. The major reaction, with phenyllithium and azobenzene for example, is the formation of a dilithium compound, for hydrolysis produces about fifty per cent of hydrazobenzene (134).

133. Fieser and Hershberg, J. Am. Chem. Soc., 62, 1640 (1940).

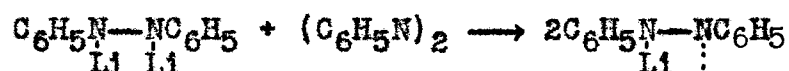
134. Gilman and Bailie, J. Org. Chem., 2, 84 (1937).



The expected addition, to yield triphenylhydrazine following hydrolysis, also takes place to a limited degree (135).



The dilithium addition compound can react with unchanged azobenzene to form a free radical (135).



The formation of the dilithium compound is smoother if hydrazobenzene is treated with methyllithium (135).

Hydrogen-metal interconversion. Metalation, the replacement of a carbon-held hydrogen by a metal, is also known as hydrogen-metal interconversion. This reaction serves some useful purposes in organic syntheses, mainly because of its ability to shorten or facilitate the production of many compounds. Since an excellent review of this general field has been made recently (136, 137) the only phases of this reaction which will be discussed are those facts which have been determined since that time regarding organolithium compounds.

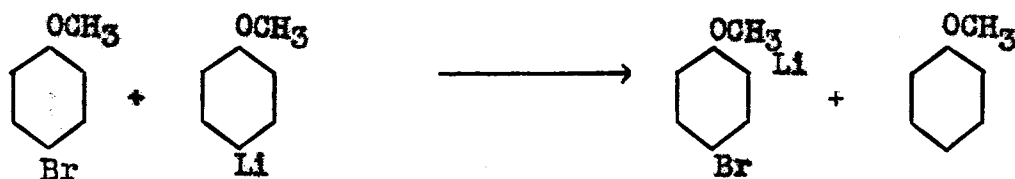
When p-bromoanisole is reacted with lithium in ether solution, the first and obvious reaction is the formation

135. Wittig, Angew. Chem., 53, 241 (1940).

136. R. L. Bebb, Doctoral Dissertation, Iowa State College, (1938).

137. Gilman and Bebb, J. Am. Chem. Soc., 61, 109 (1939).

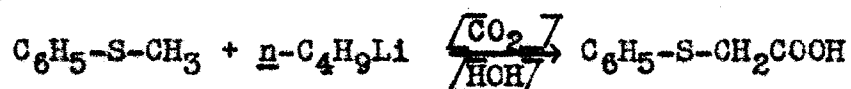
of *p*-anisyllithium. A side reaction, taking place to some extent, is the metalation of *p*-bromoanisole by the newly-formed *p*-anisyllithium (138, 82).



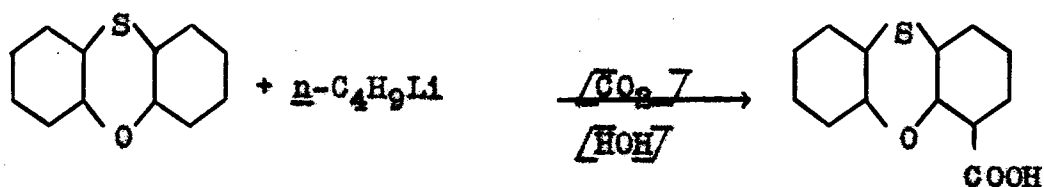
A similar reaction occurs in the preparation of *p*-phenoxyphenyllithium from *p*-bromophenyl phenyl ether (138), and in the preparation of 2-carboxydibenzofuran (139). In the latter reaction the 2-lithiodibenzofuran metalates some of the unchanged 2-bromodibenzofuran to give, subsequent to carbonation and hydrolysis, some 2-bromo-4-carboxydibenzofuran. When 3-bromodibenzofuran is treated with *n*-butyllithium in ether some 4-carboxydibenzofuran is isolated after carbonation, indicating that some of the 3-lithiodibenzofuran metalated some unchanged 3-bromo compound, being converted to dibenzofuran which is then metalated in the 4-position by *n*-butyllithium. No 3-bromo-4-carboxydibenzofuran was isolated, however (140). Organolithium compounds have been utilized in other studies on dibenzofuran (141, 142, 143).

- 138. Gilman, Langham and Jacoby, *ibid.*, 61, 106 (1939).
- 139. Gilman, Langham and Willis, *ibid.*, 62, 346 (1940).
- 140. Gilman, Willis and Swislowsky, *ibid.*, 61, 1371 (1939).
- 141. Gilman, Van Ess and Hayes, *ibid.*, 61, 643 (1939).
- 142. Gilman, Cheney and Willis, *ibid.*, 61, 951 (1939).
- 143. Gilman, Parker, Bailie and Brown, *ibid.*, 61, 2836 (1939).

When phenols and their methyl ethers are metalated, the metal does not always enter the same position in each case. For example, 4-hydroxydibenzofuran on metalation gives 6-carboxy-4-hydroxydibenzofuran, following carbonation and hydrolysis. With 4-methoxydibenzofuran, some 3-carboxy-4-methoxydibenzofuran is formed, although the 6-acid is formed in higher yield. Resorcinol gives some 2,6-dihydroxybenzoic acid with a little 2,4-dihydroxybenzoic acid. The dimethyl ether yields the 2,6-dimethoxy derivative (144). As a rule, metalation takes place ortho to the oxygen or sulfur grouping in phenols, thiophenols and their ethers. A notable exception is thioanisole, which metalates laterally (145).



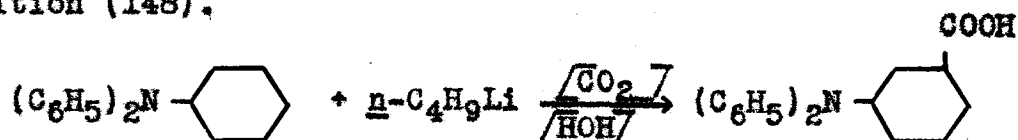
Anisole and thiophenetole metalate ortho to the ether grouping. The heterocyclic compound, phenoxathiin, also metalates ortho to the ether bridge (146).



Alcohols and amines usually are metalated in the ortho

144. Gilman, Willis, Cook, Webb and Meals, ibid., 62, 667 (1940).
145. Gilman and Webb, ibid., 62, 987 (1940).
146. Gilman, Van Rss, Willis and Stuckwisch, ibid., 62, 2606 (1940).

position. Benzyl alcohol yields o-hydroxymethylbenzoic acid after metalation with n-butyllithium followed by carbonation. Triphenylcarbinol, aniline, diphenylamine and N-n-butylaniline all metalate in a position ortho to the heteroelement (147). Surprisingly enough, triphenylamine metalates in the meta position (148).



The related triphenylphosphine also metalates in the meta position (149).

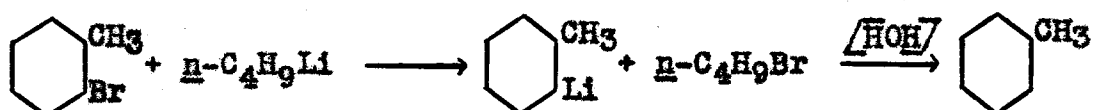
The reaction is of no value for the preparation of the simpler organolithium compounds. Toluene and n-butyllithium in ether yield only twenty-two hundredths per cent of phenylacetic acid, following carbonation and hydrolysis. Under similar conditions benzene forms fifteen per cent of benzoic acid (150).

Halogen-metal interconversion. The second type of interconversion, halogen-metal interconversion has been utilized only recently for syntheses with organolithium compounds. The earliest study on this reaction was made a number of years ago by Marvel and coworkers. Unfortunately, they allowed such long periods for reaction that only secondary products

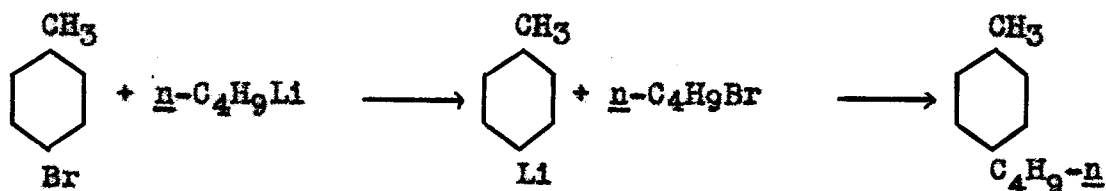
147. Gilman, Brown, Webb and Spatz, ibid., 62, 977 (1940).
148. Gilman and Brown, ibid., 62, 3208 (1940).
149. G. E. Brown, Doctoral Dissertation, Iowa State College, 1941).
150. Gilman, Pacevitz and Baine, J. Am. Chem. Soc., 62, 1514 (1940).



were obtained in most cases. Thus n-butyllithium and n-heptyl bromide in petroleum ether were allowed to stand ninety days and the mixture was then hydrolyzed. The main product was n-undecane (151). In shorter-timed reactions they did obtain products resulting from halogen-metal interconversion. For example, o-bromotoluene and n-butyllithium in petroleum ether for four days gave sixty-five per cent of toluene following hydrolysis. The reaction which occurred follows:



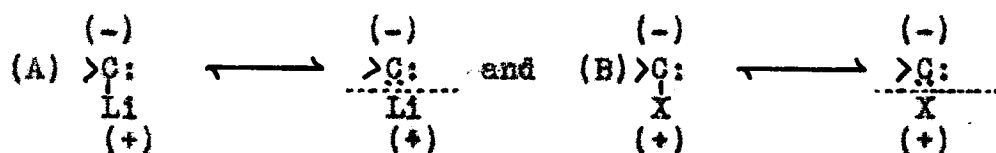
The related p-bromotoluene after thirty days yielded seventy-five per cent of p-n-butyltoluene. This reaction is similar to the one above except that in this case sufficient time elapsed before hydrolysis to permit the secondary coupling reaction to complete itself.



A similar reaction, run for twenty hours, gave an eighty-six per cent yield of p-toluic acid on carbonation (67).

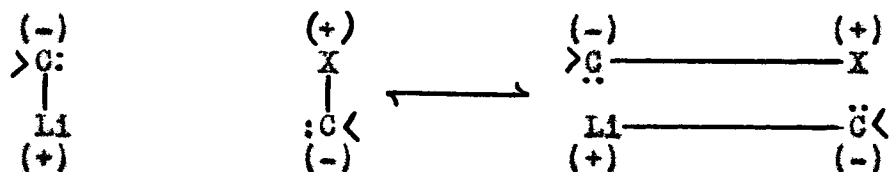
151. Marvel, Hager and Coffman, ibid., 49, 2323 (1927).

A mechanism to explain halogen-metal interconversion has been proposed recently (152) and may be outlined as follows: If two molecules, with configurations like those below, are brought in contact the two may react to form a more stable system depending upon the relative attraction of each of the charged particles for those of opposite charge. Thus, the following particles form:



Then, if the radical (B) has a greater attraction for  $Li^+$  than does (A), most of the  $Li^+$  will become attached to (B).

The following shift of bonds will then occur:



or, a halogen-metal interconversion will take place. That the secondary coupling observed, especially in longer-timed reactions, is not the final step of this process, but another reaction entirely, is based on the fact that  $X^+$  and  $Li^+$  do not combine to form  $LiX$ . That is, the positive halogen postulated cannot react with the lithium ion. The basis of this whole mechanism rests on the ionization of the halogen

152. Meerwein, Hofmann and Schill, J. prakt. Chem., 154, 266 (1940).

lacking an electron pair. This is not the usual manner of ionization of halogen. Some reactions, however, indicate that such ionizations do occur.

Other factors than time affect the extent of halogen-metal interconversion and a systematic study of some of these has recently been reported (153). The factors studied were solvent, temperature, kind of organolithium compound, concentration of reactants and catalytic agents. The rate is affected greatly by the nature of the solvent. Thus, in the polar solvents, like diethyl ether, dibutyl ether and dimethylaniline, the reaction between  $\alpha$ -bromonaphthalene and *n*-butyllithium is very rapid, maximum yields of interconversion product,  $\alpha$ -naphthyllithium, being obtained in a period of only a few minutes. In non-polar solvents, like benzene, cyclohexane and petroleum ether, the reaction is slower and less complete in the same time periods. The use of petroleum ether as a solvent for these reactions is recommended, however, because the secondary coupling reaction seems to be strongly inhibited in this solvent (67). Small temperature changes do not alter the rate of reaction in ether appreciably. Cooling to  $-80^{\circ}$  gives a much slower rate of reaction than that observed at room temperature and is of little value except in special cases (153, 154) where

153. Gilman and Moore, J. Am. Chem. Soc., 62, 1843 (1940).  
154. Gilman and Spatz, ibid., 62, 446 (1940).

preferential reaction is desired with polyfunctional compounds. The kind of organolithium compound is an important factor, for with  $\alpha$ -bromonaphthalene in ether the order of decreasing effectiveness was found to be n-propyl-, ethyl-, n-butyl-, phenyl-, and methyllithium. Of these, methyllithium gives only a trace of interconversion product. The concentration of reactants is not so important, although the reaction is more rapid at moderately high concentrations than in more dilute solutions. No really effective catalyst has been found. Copper bronze has some beneficial effect, whereas Raney nickel decreases the yields slightly.

The rate and extent of interconversion is also dependent upon the nature of the halide used. The reaction of aryl iodides is very fast and aryl bromides are slower. This is evidenced by the instantaneous reaction between o-iodoanisole and phenyllithium in ether whereas o-bromoanisole requires about an hour (135). Only a few isolated cases of chlorine- or fluorine-metal interconversion have been observed. The compounds known to give this reaction at the present time are o-chloro- and o-fluoroanisole with phenyllithium (135) and phenylethynyl chloride (155) and 3-chloro-2,4,5-triphenylfuran (156) with n-butyllithium.

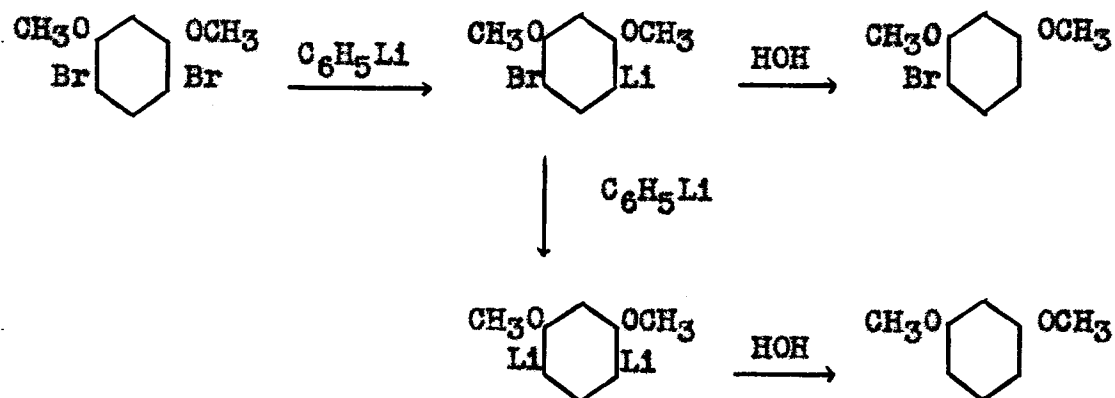
155. Unpublished studies by A. H. Haubein.

156. Unpublished studies by D. S. Melstrom.

The halogen-metal interconversion is probably not an intermediate step in coupling reactions, as was mentioned above. Although coupling is favored when the RX compound is an alkyl bromide or iodide the following facts demonstrate that this is only a minor point. First, no evidence of halogen-metal interconversion between alkyl halides and aryllithium compounds has, as yet, been obtained. Second, only a few isolated cases of chlorine- or fluorine-metal interconversion have been found and most aryl chlorides and fluorides do not give this reaction under conditions tried thus far. Third, no halogen-metal interchange has been obtained with organolithium compounds like phenylethynyllithium ( $\text{C}_6\text{H}_5\text{C}\equiv\text{CLi}$ ). Fourth, the slow rate of interconversion exhibited by the less reactive organomagnesium and -aluminum compounds makes it appear unlikely that any possibly intermediately formed organocopper and organonickel compounds take part in interconversion reactions when copper and nickel are used to produce coupling of halides.

The halogen-metal interconversion reaction has been used to obtain some compounds which are otherwise rather inaccessible. Its use to prepare compounds like  $\alpha$ -naphthyllithium (153) or *p*-anisyllithium (138) is not recommended since the direct preparation of these compounds is equally satisfactory and less expensive. It is, however, very useful in preparing more complex compounds. If 1,3-dimethoxy-

4,6-dibromobenzene is treated with one equivalent of phenyllithium in ether for a short time, only one of the bromines is replaced (82).



If two equivalents of phenyllithium are used, partial interconversion of both bromines takes place. For example, after an eighteen hour reaction period, hydrolysis yielded seventy-two per cent of 1,3-dimethoxybenzene, eight per cent of 1,3-dimethoxy-4-bromobenzene and sixty per cent of bromobenzene (157). When 2-bromodibenzofuran is treated with *n*-butyllithium in ether for thirty minutes an eighty-seven per cent yield of 2-carboxydibenzofuran is obtained following carbonation (139). 4-Bromodibenzofuran also undergoes this reaction with *n*-butyllithium (140). Other bromodibenzofurans have also been reacted in this manner (158). A reaction between bromo-

157. Wittig and Pockels, *Ber.*, **72**, 89 (1939).

158. Gilman, Swislowky and Brown, *J. Am. Chem. Soc.*, **62**, 348 (1940).

form and phenyllithium in equivalent quantities in ether gave bromobenzene and some stilbene when hydrolyzed after twenty minutes (159). A reaction between bis (4-chloromethylphenyl)methane and phenyllithium gave only resinous materials along with biphenyl (160). Hexabromobenzene and phenyllithium also yield resinous substances (161).

A recent application of halogen-metal interconversion has made use of this reaction to establish the structures of some substituted 2,2'-dihydroxybiphenyls (162). Thus, the X,X'-dibromo-2,2'-dihydroxybiphenyl of earlier workers was shown to be the 5,5'-dibromo-2,2'-dihydroxybiphenyl by halogen-metal interconversion of the dibromo-2,2'-dimethoxybiphenyl with n-butyllithium, followed by carbonation to the known 5,5'-dicarboxy-2,2'-dimethoxybiphenyl. This proof was supplemented by another, not dependent on halogen-metal interconversion, showing that the method is reliable. Other similar proofs were also carried out.

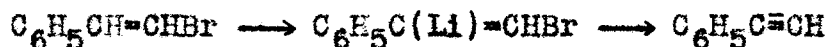
The halogen-metal interconversion reaction between  $\beta$ -bromostyrene and n-butyllithium is of special interest since it involves an aliphatic halogen compound and leads to the relatively rare type of vinyl- or substituted vinyl-lithium compound. In the first study of this reaction (151)

- 159. Wittig and Pockels, Ber., 72, 884 (1939).
- 160. Connerade, Bull. soc. chim. Belg., 44, 411 (1935).
- 161. Geissman and Mallatt, J. Am. Chem. Soc., 61, 1788 (1939).
- 162. Gilman, Swiss and Cheney, ibid., 62, 1963 (1940).

the reactants were allowed to stand thirty-eight days in a sealed tube in petroleum ether solution. Hydrolysis produced 1-phenyl-1-hexene and 1,4-diphenyl-1,3-butadiene. No evidence of the formation of octane, phenylethylene or phenylacetylene was found. A similar reaction, run for twenty hours at reflux, was carbonated and a twenty-three per cent yield of trans-cinnamic acid was obtained. In diethyl ether, the products of carbonation are somewhat different. In addition to trans-cinnamic acid, phenylpropionic acid is also obtained (67). Two possible mechanisms for this reaction have been proposed. First, the n-butyllithium may have split out hydrogen bromide from the  $\beta$ -bromostyrene, forming phenylacetylene, which then undergoes metalation to form phenylethynyllithium.



Second, there may have been lateral metalation followed by loss of lithium bromide, to form phenylacetylene which then undergoes metalation.



No conclusive evidence of either mechanism has, as yet, been obtained. Similar mechanisms would account for these same products which are obtained when  $\beta$ -styryllithium from  $\beta$ -bromostyrene and lithium in ether, is carbonated (53).

Bromodimethylanilines undergo halogen-metal interconversion with n-butyllithium. m-Bromodimethylaniline yields



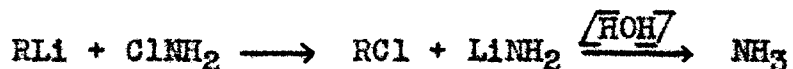
twenty-six per cent of the corresponding acid following carbonation after twenty hours, while the para isomer yields forty-five per cent under the same conditions (163). This latter compound has been recently proposed as a reagent for qualitatively detecting active organometallic compounds (164). Under conditions where n-butyllithium gives a positive test, n-butylmagnesium bromide does not give a positive reaction. The basis of the test is the fact that organolithium compounds undergo halogen-metal interconversion with p-bromodimethylaniline whereas organomagnesium halides have not given this reaction under the same conditions. Lithium compounds of pyridine and quinoline have also been obtained by this reaction. For example, 3-bromoquinoline and n-butyllithium in ether at  $-35^{\circ}$  yield fifty-two per cent of 3-carboxyquinoline after carbonation at the end of a fifteen minute reaction period (154). Addition of the organolithium compound to the anil linkage does not take place quantitatively under these conditions, but the addition compound is formed in relatively high yield.

Halogens attached to nitrogen appear to undergo halogen-metal interconversion with organolithium compounds. In reactions of monochloroamine with various organolithium compounds, poor yields of amines but fairly good yields of ammonia were

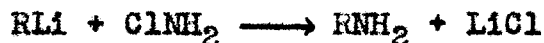
163. Gilman and Banner, ibid., 62, 344 (1940).

164. Gilman and Swiss, ibid., 62, 1847 (1940).

obtained (165). These results indicate that the principal reaction was as follows:

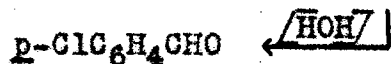


The reaction expected was coupling in the following manner:



With phenyllithium, for example, the yields at 0° were three per cent aniline and forty-eight per cent ammonia. When three equivalents of phenyllithium were used, the yields were ten per cent aniline and forty-two per cent ammonia. At -50°, with three equivalents, the yields were thirty-three and thirty-seven per cent, respectively. These results show that there is some correlation between this reaction and the halogen-metal interconversion between  $\alpha$ -bromonaphthalene and organolithium compounds (see page 63).

Ald-chlorimines also show this reaction to a certain extent. The mechanism proposed for this reaction (166) also involves the removal of a positive halogen (see page 62). For example, 4-chlorobenzalchlorimine and phenyllithium react in ether solution in two ways, namely:



165. Coleman, Hermanson and Johnson, *ibid.*, 59, 1896 (1937).
166. Le Maistre, Rainsford and Hauser, *J. Org. Chem.*, 4, 106 (1939).

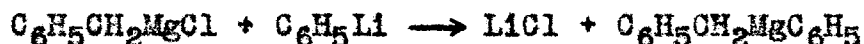
The first reaction involves the removal of hydrogen chloride, the second is a halogen-metal interconversion in which a chlorine with a sextet of electrons is removed. Grignard reagents also give this reaction. Comparing phenyllithium and phenylmagnesium bromide as regards their reaction with *p*-chlorobenzalchlorimine under the same conditions, phenyllithium yields twenty per cent *p*-chlorobenzonitrile and thirty-four per cent *p*-chlorobenzaldehyde while with phenylmagnesium bromide the yields are ten and sixty-one per cent, respectively. From this it is evident that phenyllithium reacts according to the second equation to a lesser extent than phenylmagnesium bromide but this does not prove that the Grignard reagent is better than phenyllithium for halogen-metal interconversion with such nitrogen compounds since the other reaction introduces a complicating factor. Reaction of unchanged organometallic compound with the nitrile formed would also alter the ratio of products. To what extent, if any, this reaction occurs is not known.

Metal-metal interconversion. The third type of interconversion, metal-metal, is known to occur with many different organometallic compounds. The general reaction may be written as follows:



One of the first applications of this method to the preparation of organolithium compounds was made by Ziegler (71)

who treated dibenzylmercury with n-butyllithium obtaining di-n-butylmercury and benzyllithium. He later extended this reaction to the Grignard reagent in order to prepare the less accessible organolithium compounds like benzyllithium and iso-propyllithium (47). The reaction, in the case of benzylmagnesium chloride, proceeds as follows:



This reaction is not very useful for the preparation of organolithium compounds since it also forms organomagnesium compounds which often interfere in subsequent reactions.

Austin noted that in reactions of organolithium compounds with organolead halides, an excess of the organolithium compound was detrimental to the preparation of the unsymmetrical compounds because the organolithium compound displaced some of the original groups attached to lead (167). In a reaction between tetraethyllead and p-tolyllithium, however, he was unable to isolate any p-tolyllead compounds.

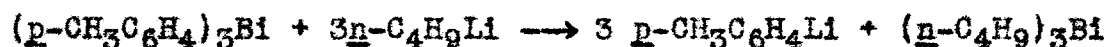
Organoboron compounds like trimethylboron (4) and tri-n-butylboron (168) do not react with phenyllithium to give any phenylboron compounds although an exothermic reaction occurs. With ethyllithium an addition compound,  $\text{C}_2\text{H}_5\text{Li} \cdot \text{B}(\text{CH}_3)_3$ , forms. This is thought to be a compound of the

167. Austin, J. Am. Chem. Soc., 54, 3726 (1932).

168. Johnson, Snyder and Van Campen, ibid., 60, 115 (1938).

type  $M^+/\overline{BR_4^-}$ . When diborane is treated with ethyllithium the substance formed is lithium borohydride (169).

The metal-metal interconversion reaction has been extended to compounds of bismuth. For example, tri-*p*-tolylbismuth and *n*-butyllithium in ether solution yield seventy per cent of *p*-toluic acid after carbonation. The reaction follows (170):



The extent of reaction is estimated by carbonating the organolithium compound and isolating the resulting acid.

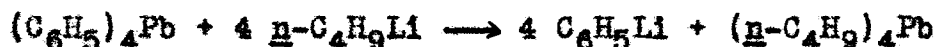
Organothallium compounds react in a similar manner (171).

A recent study of this reaction between organolead and organolithium compounds has been reported (172).

Although the metal-metal interconversion reaction has not been widely applicable to the preparation of organolithium compounds it does serve some useful purposes. For example, although organometallic radicals, like triphenyllead, are thought to be more reactive than the corresponding compounds, like tetraphenyllead, which have the metal in a normal valence state, no means of determining this relative reactivity has been possible until recently. In these cases, neither the radicals nor normal compounds have been sufficiently

169. Schlesinger and Brown, *ibid.*, **62**, 3429 (1940).  
170. Gilman, Yablunsky and Svigoon, *ibid.*, **61**, 1170 (1939).  
171. Gilman and Jones, *ibid.*, **62**, 2357 (1940).  
172. Gilman and Moore, *ibid.*, **62**, 3206 (1940).

reactive to combine with functional groups, like the carbonyl. The recent study by Gilman and Jones (171) on the more rapid addition of phenylthallium over triphenylthallium to some functional groups is the first reported case of a distinctly reactive organometallic radical. A reaction was needed, therefore, which could be used to determine the relative firmness of attachment of R groups to M in compounds like  $R_3M$  and  $R_4M$ , where  $R_3M$  is the compound with abnormal valence. The metal-metal interconversion reaction serves this purpose as is shown by the following observations: Tetraphenyllead reacts with n-butyllithium in ether solution at a fairly rapid rate as follows:



As with the bismuth compounds, the phenyllithium is readily estimated, after carbonation, as benzoic acid, and the tetra-n-butyllead can be isolated. Triphenyllead reacts more rapidly in an apparently analogous manner. By comparing the respective yields of benzoic acid obtained under the same conditions of reaction an estimate of the relative firmness of attachment of the phenyl group to lead in triphenyllead and in tetraphenyllead is obtained. In such a manner it was found that triphenyllead undergoes interconversion with n-butyllithium more rapidly than tetraphenyllead, for, where no benzoic acid was obtained with the latter compound, the former gave thirteen per cent of

the acid in a short time reaction. Similarly, it was shown that tri-p-tolyllead is more reactive than tetra-p-tolyllead in this type of interconversion.

A more complete survey of the relative reactivities of organolithium compounds in various types of reaction is given in the Discussion.

Another interesting application of the metal-metal interconversion has been made by Ziegler (68) as a means of analyzing solutions of alkyllithium compounds which contain colloidal metal or inorganic lithium compounds, like lithium oxide or nitride which react with water to form lithium hydroxide. When these impurities are present, the determination of the titer of solution by the acid-titration method (69) is meaningless, because the value so obtained is due not only to the organolithium compound but also to the inorganic compounds just mentioned. To avoid this difficulty Ziegler took advantage of two facts about organolithium compounds which had been determined. First dibenzylmercury undergoes metal-metal interconversion with alkyllithium compounds forming benzylolithium and dialkylmercury compounds. Second, although the alkyllithium compounds react only very slowly with alkyl halides, benzylolithium reacts very rapidly with them to form hydrocarbons and lithium halides. Briefly, his method of analysis is to treat an aliquot of the alkyllithium solution with excess

n-butyl bromide and then with dibenzylmercury in small portions. When the yellow color, due to benzyllithium, fails to appear on the addition of a portion of the mercurial the reaction is complete. The lithium bromide thus formed is determined by a Volhard analysis and the amount of alkyl-lithium compound can then be calculated. The reactions involved are shown below:

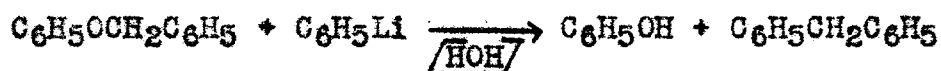


Other cleavage reactions. Organolithium compounds cleave other types of linkages in addition to those mentioned above in interconversion reactions. One of the most important of these types is the carbon-oxygen linkage found in ethers. It is more unfortunate that a solvent like diethyl ether, which facilitates so many reactions of organolithium compounds, should also react with them. A knowledge of the rates of cleavage of this solvent by various organolithium compounds would be most helpful in many ways. The only quantitative study which has been reported (68) is the reaction of n-butyllithium with ether in a mixture of ether and benzene. The cleavage becomes a matter of importance after about four hours, the concentration of n-butyllithium decreasing to one-third its original value in forty-eight hours. Organolithium compounds like 9-phenanthryllithium and  $\alpha$ -naphthyllithium are reported to cleave ether rapidly but no data



are given (83). There is some question as to just what is meant by "rapidly" for the results on the interconversion of  $\alpha$ -bromonaphthalene (153) and of some bromophenanthrenes (173) indicate that the term cannot mean less than a few hours. The only organolithium compound known to cleave ether in a matter of minutes is t-butyllithium. iso-Propyl- and s-butyllithium cleave it more slowly (174).

Phenyllithium has been used as a reagent for cleaving some mixed aromatic aliphatic ethers such as phenyl allyl ether and phenyl benzyl ether while others like anisole and phenyl n-butyl ether are not appreciably affected, even after several days (175). Diethyl ether is also slowly cleaved by phenyllithium. When cleavage occurs the aliphatic group is removed. This is illustrated for phenyl benzyl ether by the following equation:



Ethylene oxide, a cyclic ether, reacts with organolithium compounds, as with the Grignard reagent, to give  $\beta$ -hydroxyethyl derivatives. Thus 4-dibenzofuryllithium and ethylene oxide yield 4-( $\beta$ -hydroxyethyl)dibenzofuran (176). It was noted above that under certain conditions the cyclic ether grouping in  $\alpha$ -oxido ketones does not react with organolithium

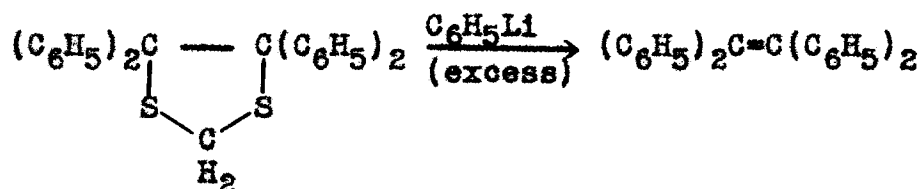
- 173. Gilman and Cook, J. Am. Chem. Soc., 62, 2813 (1940).
- 174. Unpublished studies by the author.
- 175. Lüttringhaus and Sääf, Angew. Chem., 51, 915 (1938).
- 176. Kirkpatrick and Parker, J. Am. Chem. Soc., 57, 1123 (1935).

compounds (see page 48).

Organic sulfur compounds are also cleaved by organolithium compounds. The disulfides react in the following manner.



This reaction serves as a method for obtaining unsymmetrical thioethers (177). The reaction has been extended to the diselenides (178). Other more complex compounds of sulfur have also been cleaved by organolithium compounds. A single illustration (179) will suffice for all these (180, 181).



Coupling reactions. As was mentioned in connection with halogen-metal interconversion, the reaction of organolithium compounds and organic halides usually leads to coupling products if allowed sufficient time for reaction. This fact is demonstrated by the results of Marvel (151). Other reactions giving coupling products have been run. 9-Fluorenyllithium reacts with n-butyl bromide to give 9-n-butylfluorene in

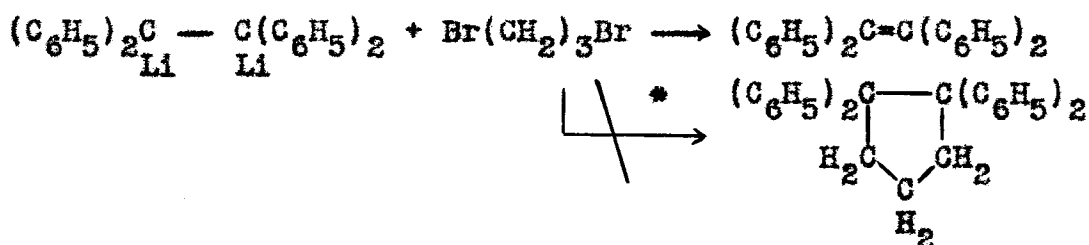
177. Schönberg and v. Vargha, Ber., 64, 1390 (1931).
178. Schönberg, Stephenson, Kaltschmitt, Petersen and Schulten, ibid., 66, 237 (1933).
179. Schönberg, Cernik and Urban, ibid., 64, 2577 (1931).
180. Schönberg and Nickel, ibid., 64, 2323 (1931).
181. Schönberg, Kaltschmitt and Schulten, ibid., 66, 245 (1933).

forty-one per cent yield (59) and with benzohydril chloride to give 9-benzohydrilfluorene (182). Indenyllithium and 1-chlorohydrindene couple to form 1-(1-indenyl)hydrindene (183) while 2,3-diphenylindenyllithium and benzyl chloride yield the corresponding 1-benzyl compound (184). *p*-Bromo-*t*-butylbenzene and phenyllithium give a five per cent yield of *p-t*-butylbiphenyl (185). When  $\alpha$ - and  $\beta$ -halogenonaphthalenes are reacted with lithium in ether and the resultant solutions are treated with dimethyl sulfate and hydrolyzed, good yields of methylnaphthalenes are obtained (186).  $\alpha$ -Picollythium and ethyl bromide yield conyrene (187).

The lithium compounds formed by the action of lithium metal or organolithium compounds on nitrogen-nitrogen double bonds also give coupling products with some reactants. The dilithium compound of azobenzene (see page 56) reacts with dimethyl sulfate to form *N,N'*-dimethylhydrazobenzene and with 1,3-dibromopropane to give *N,N'*-diphenylpyrazolidine (135). This coupling reaction, to form a five-membered ring, is different from the reaction of most of the dilithium compounds formed by metal addition to ethylenic linkages in that

- 182. Bergmann, *ibid.*, 63, 1617 (1930).
- 183. Bergmann and Taubadel, *ibid.*, 65, 463 (1932).
- 184. Blum-Bergmann, *ibid.*, 65, 109 (1932).
- 185. v. Grosse, Mavity and Ipatieff, *J. Org. Chem.*, 3, 448 (1938).
- 186. Vesely and Stursa, *Chem. Listy*, 26, 495 (1932) [*C.A.*, 27, 717 (1933)].
- 187. Bergmann and Rosenthal, *J. prakt. Chem.*, 135, 267 (1932).

the reaction of 1,3-dibromopropane simply removes the metal atoms in the latter cases. For example 1,2-dilithio-1,1,2,2-tetraphenylethane and 1,3-dibromopropane yield 1,1,2,2-tetraphenylethylene instead of the expected 1,1,2,2-tetraphenylcyclopentane (2).



The reaction of organolithium compounds with acid halides usually results in a tertiary carbinol. If the organolithium compound is of a low order of reactivity, ketones may be formed. For example, 9-fluorenyllithium and benzoyl chloride form 9-benzoylfluorene and/or 9,9-dibenzoylfluorene, the latter resulting from secondary reactions (188, 189, 190). With acetyl chloride 9-acetylfluorene results (59).  $\alpha$ -Picolyl-lithium and benzoyl chloride react to form  $\alpha$ -phenacylpyridine which soon decomposes (187). If 2,7-dimethyl-4-bromohydrindene is treated with lithium in ether and  $\alpha$ -naphthoyl chloride is added, a compound, thought to be 2,7-dimethyl-4-(1-naphthoyl)hydrindene, is one of the products isolated following hydrolysis.

188. Schlenk and Bergmann, Ber., 62, 745 (1929).

189. Pfeiffer and Lübke, ibid., 63, 762 (1930).

190. Kliegl, Weng and Wiest, ibid., 63, 1262 (1930).

\* The diagonal line signifies that the reaction does not follow the course indicated.

Another rather surprising product obtained in this reaction is  $\alpha$ -naphthoic anhydride (55).

Reactions with salts. Inorganic halides react with organolithium compounds to form less reactive organometallic compounds. The general reaction may be written as follows:

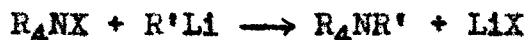


There are several examples of this reaction. Benzyl lithium reacts with mercuric chloride to form dibenzylmercury (43). Phenyllithium and cadmium chloride (191) or bromide (192) yield diphenylcadmium. *p*-Dimethylaminophenyllithium and magnesium iodide yield *p*-dimethylaminophenylmagnesium iodide (193). Organothallium compounds have been prepared by a number of investigators using this method. Thallous chloride (171, 194, 195), thallic chloride (195) and organothallium chlorides (171, 194, 195, 196, 197, 198) have been used. Lead chloride, stannic chloride and organolead halides react with organolithium compounds to form simple compounds of these metals (167, 199). In some cases the end product is not the compound having the metal in its normal valence state

191. Gilman and Nelson, Rec. trav. chim., 55, 518 (1936).
192. Nesmeyanov and Makarova, J. Gen. Chem. (U.S.S.R.) 7, 2649 (1937) [C.A., 32, 2095 (1938)].
193. Unpublished studies by R. H. Kirby.
194. Birch, J. Chem. Soc., 1132 (1934).
195. Melnikov and Gracheva, J. Gen. Chem. (U.S.S.R.) 6, 634 (1936) [C.A., 30, 5557 (1936)].
196. Groll, J. Am. Chem. Soc., 52, 2998 (1930).
197. Rochow and Dennis, ibid., 57, 486 (1935).
198. Gilman and Jones, ibid., 61, 1513 (1939).
199. Gilman and Towne, ibid., 61, 739 (1939).

but is an organometallic radical. Thus,  $\alpha$ -naphthyllithium and lead chloride yield six to ten per cent of tri- $\alpha$ -naphthyllead under special conditions (200). The reaction of an organolead halide with an optically active organolithium compound has been carried out. Unfortunately, the organolead compound formed, which should exist in two diastereoisomeric forms, could not be resolved (62).

Various attempts have been made to prepare nitrogen compounds in which five hydrocarbon groups are attached to the nitrogen atom. Some organolithium compounds have been used in one of these studies. Marvel and coworkers have reacted quaternary ammonium compounds with organolithium compounds in the hope that the following reaction would take place (44):

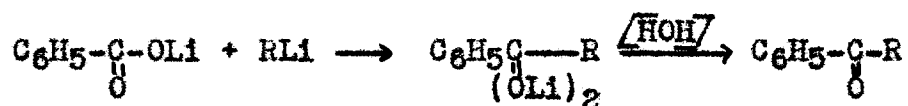


This reaction did not take place. As end products, tertiary amines and hydrocarbons were obtained. In no case did the tertiary amine contain an R group that was not present in the quaternary salt, indicating that intermediate formation of  $R_4NR'$ , followed by decomposition, probably did not occur. This reaction was extended to the corresponding phosphonium (201) and arsonium (73)

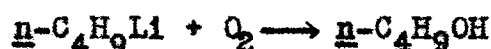
200. Gilman and Baillie, ibid., 61, 731 (1939).

201. Coffman and Marvel, ibid., 51, 3496 (1929).

compounds with similar results. Tungsten hexachloride and phenyllithium react to form, after hydrolysis, compounds with the formulas  $(C_6H_5W)_2O_7H_4$  and  $(C_6H_5)_3W_2O_8H_7$ . Not much is known of the nature of these compounds (202). Some organic salts, such as lithium benzoate, react with organolithium compounds to give good yields of ketones (111).



Miscellaneous reactions. Mention has been made of the necessity of preparing and manipulating organolithium compounds in an inert atmosphere free of carbon dioxide, oxygen and water vapor. The reaction of organolithium compounds with the first of these substances has already been discussed. With oxygen the products are not so definite, being dependent on such factors as the nature of the organolithium compound and solvent. When alkylolithium compounds are oxidized by dry air, good yields of the corresponding alcohols are obtained. n-Butyllithium yields seventy-five per cent of n-butanol in this reaction (83).



The aryllithium compounds are more erratic. In ether solution phenyllithium gives only eighteen per cent of phenol and sixty-four per cent of biphenyl. Other aryllithium compounds

202. Hein and Nebe, Naturwissenschaften, 28, 93 (1940).

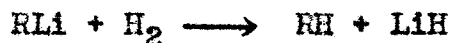
give similar high yields of coupling products (83). If the ether is completely removed before oxidation the yields of phenol and coupling product are practically equal. Ether-free phenyllithium yields twenty-five per cent of phenol and of biphenyl (203). When phenyllithium is oxidized with tetralin peroxide in ether solution a ninety per cent yield of phenol is obtained (83).

Organolithium compounds act as dehydrogenating agents in some cases. Phenyllithium or *n*-butyllithium convert 1,4-dihydrodibenzofuran to dibenzofuran. 1,4-Dihydronaphthalene and 1,4-diphenyl-2-butene are also dehydrogenated by these reagents (204), as is 1,4-dihydrodibenzothiophene (205). 1,2,3,4-Tetrahydrodibenzofuran, however, yields about five per cent of the 6-acid with phenyl- or *p*-tolyllithium (206). Dehydrogenation was not observed in this case. This removal of hydrogen was also noted in the reaction of phenyllithium with 8-phenyl-9-methoxy-peri-naphthindan-7-one (see page 43). When organolithium compounds are treated with hydrogen, reduction to hydrocarbons results (207). The rate of reduction is not affected by such substances as platinum and palladium which usually facilitate reductions with hydrogen.

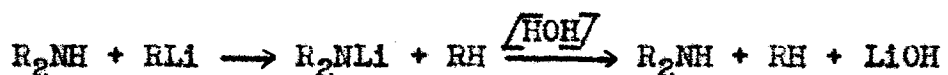
- 203. Pacevitz and Gilman, J. Am. Chem. Soc., 61, 1603 (1939).
- 204. Gilman and Bradley, ibid., 60, 2333 (1938).
- 205. Gilman and Jacoby, J. Org. Chem., 3, 108 (1938).
- 206. Gilman, Smith and Cheney, J. Am. Chem. Soc., 57, 2095 (1935).
- 207. Gilman, Jacoby and Ludeman, ibid., 60, 2336 (1938).



The reaction proceeds as follows:



With water the organolithium compounds yield hydrocarbons and lithium hydroxide. Similarly, with secondary amines the reaction results in a hydrocarbon and a disubstituted lithium amide (126, 208). The general reaction follows:



The reactions with hydrogen, water and secondary amines are obviously similar in that they all produce hydrocarbons. These reactions are not of great value in syntheses.

There are a number of miscellaneous reactions of minor importance shown by organolithium compounds. Carbon disulfide reacts with organolithium compounds to give sulfur analogs of carboxylic acids (178).



Phenyllithium reacts with methoxyamine at  $-10$  to  $-15^\circ$  to form aniline in sixty-three per cent yield (209). When some organometallic compounds react with nitrogen trioxide, diazonium compounds are formed, but the organolithium compounds do not give this reaction (197). Phenyllithium, when heated for four to two hundred hours in ether or xylene with

208. Ziegler, Eberle and Ohlinger, *Ann.*, 504, 94 (1933).

209. Sheverdina and Kocheshkov, *J. Gen. Chem.*, (U.S.S.R.), 8, 1825 (1938) [*C.A.*, 33, 5804 (1939)].

metals like magnesium, mercury, tin and lead, forms as high as twenty-seven per cent of the phenyl compounds of these metals (48). Strangely enough, n-butyllithium is not affected by two or forty per cent sodium amalgams (42).

Carbon monoxide is reported to react with phenyllithium to give  $\omega,\omega$ -diphenylacetophenone (135) but no details are given. The reaction of carbon monoxide with the corresponding Grignard reagent takes place at higher temperatures to form benzil (211).

With N-methylformanilide, 2,6-dimethoxyphenyllithium reacts to yield 2,6-dimethoxybenzaldehyde in good yield (135).

210. Makarova and Nesmeyanov, J. Gen. Chem. (U.S.S.R.), 2, 771 (1939); C.A., 34, 391 (1940)/.
211. Fischer and Stoffers, Ann., 500, 253 (1933).

## EXPERIMENTAL

### Preparation of Alkylolithium Compounds

The preparation of organolithium compounds in diethyl ether solutions has been adequately described by earlier workers (42, 51). No significant changes in either technique or yields have been made since these comprehensive studies were reported.

It has recently been demonstrated (67) that petroleum ether, boiling point 28-38°, is an excellent solvent in which to prepare the lower alkylolithium compounds by the reaction between alkyl halides and lithium metal. The technique involved in this method is somewhat different than that used for the preparations in diethyl ether, so a general procedure is given at this point.

The conventional apparatus, consisting of a two hundred fifty ml. three-necked flask fitted with gas-tight mechanical stirrer, reflux condenser and dropping funnel, is flushed with dry nitrogen, free of oxygen and carbon dioxide. Fifty ml. of dry, "unsaturate-free" petroleum ether (b.p. 28-38°) is placed in the flask. Slightly more than seven-tenths gram of lithium is rasped (67) directly into the flask, through a paper cone or funnel, in an emerging stream of nitrogen.

Five-hundredths mole of the desired alkyl halide (the chlorides give best yields), dissolved in fifty ml. of solvent, is placed in the dropping funnel. The reaction vessel is heated until the solvent refluxes gently and the halide solution is dropped in slowly, with rapid stirring. The reaction soon starts, as is evidenced by an increase in the rate of reflux and the appearance of the lithium particles. These particles soon become somewhat blue in color and no longer float on the surface of the solvent. The halide is added over a period of about an hour. After the addition is completed, refluxing and stirring are continued until no evidence of reaction is visible. This is easily determined by removing the heat source and stopping the stirrer. If unreacted halide remains, its reaction with the lithium causes a bubbling of the solvent around the lithium. If no bubbling is observed the reaction is substantially complete. The reaction mixture is allowed to stand, under nitrogen, to allow the suspended material to settle. Standing overnight is recommended to insure complete removal of organic halide. The supernatant liquid is decanted into the filtration apparatus (67) and filtered. The volume of filtrate is adjusted to one hundred ml. by addition of solvent and an aliquot is removed and hydrolyzed. Titration of this hydrolyzed portion with standard acid permits the determination of the concentration of alkyllithium compound and the yield obtained. The

residue from the reaction is conveniently disposed of by adding it, in small portions, to a large volume of water in a well-ventilated hood.

This method has been used successfully with the lower alkyl halides including n-amyl chloride. Methyllithium cannot be prepared in this manner because of its insolubility in the petroleum ether. Ethyllithium appears to be of limited solubility, also.

The yields of alkyllithium compounds obtained by the above method are given in Table I.

Table I

Yields of Some Alkyllithium Compounds in Petroleum Ether

<u>Halide used</u>	<u>% Yield</u>
Ethyl Bromide	50
<u>n</u> -Propyl Bromide	60
<u>n</u> -Propyl Chloride	85
<u>iso</u> -Propyl Bromide	15
<u>iso</u> -Propyl Chloride	75
<u>n</u> -Butyl Bromide	70
<u>n</u> -Butyl Chloride	85
<u>iso</u> -Butyl Chloride	85
<u>s</u> -Butyl Chloride	85
<u>t</u> -Butyl Chloride	50
<u>n</u> -Amyl Chloride	85

The preparation of t-butyllithium demands special care. The t-butyl chloride used must be scrupulously purified and dried before use. Redistillation just before use is recommended. The preparation, at the present time, is very erratic and highly remindful of the similar preparation of t-butyl-magnesium chloride.

The values in the above table are the yields to be expected under ordinary conditions. With somewhat slower addition of the halide solution, higher yields are often obtained. The yields in larger-sized preparations may be somewhat lower.

#### Factors Affecting Halogen-Metal Interconversion

The effects of most of the important factors in halogen-metal interconversion already have been reported (67, 153). The further investigations made on the nature of the reactants are given here.

#### $\alpha$ -Bromonaphthalene and n-amyllithium.

Ziegler has observed that n-propyllithium adds to 1,1-diphenylethylene more rapidly than ethyl- or n-butyllithium (68). Since n-propyllithium also appeared more effective than ethyl- and n-butyllithium in halogen-metal interconversion it seemed worthwhile to try n-amyllithium in this latter reaction to see if the alkylolithium compounds with an odd number of carbons were more effective than those with an even number of carbons.

An equivalent quantity of  $\alpha$ -bromonaphthalene was added to a 0.25 molar solution of n-amyllithium in ether. The solution was stirred at room temperature and aliquots were removed

and carbonated at time intervals corresponding to those used for the other reactions (153). The results of this experiment are given below in Table II.

Table II

Yields of  $\alpha$ -Naphthoic Acid from  $\alpha$ -Bromonaphthalene and n-Anyllithium

<u>Time (min.)</u>	<u>Yield %</u>
0.5	58
1.0	59
5.0	58
10.	47
30.	36

$\alpha$ -Bromonaphthalene and isomeric alkyllithium compounds.

In order to compare the relative reactivities of various isomeric alkyllithium compounds in halogen-metal interconversion the action of these compounds on  $\alpha$ -bromonaphthalene was examined. Low-boiling petroleum ether was used as solvent to avoid complicating side reactions such as cleavage. An equivalent quantity of  $\alpha$ -bromonaphthalene was added to a 0.25 molar solution of each of the alkyllithium compounds listed in Table III. Aliquots were removed and carbonated as usual, the yields being calculated from the weights of  $\alpha$ -naphthoic acid isolated.

Table III

Yields of  $\alpha$ -Naphthoic Acid from  $\alpha$ -Bromonaphthalene and Isomeric Alkylolithium Compounds in Petroleum Ether

Time (min.)	<u>n-C<sub>3</sub>H<sub>7</sub>Li</u>	<u>iso-C<sub>3</sub>H<sub>7</sub>Li</u>	<u>n-C<sub>4</sub>H<sub>9</sub>Li</u>	<u>iso-C<sub>4</sub>H<sub>9</sub>Li</u>	<u>s-C<sub>4</sub>H<sub>9</sub>Li</u>	<u>t-C<sub>4</sub>H<sub>9</sub>Li</u>
15			10	13	77	26
30	11	71	17	16	81	32
60	18	78	27	24	80	34
120	21	47	40	35	63	30

$\alpha$ -Bromonaphthalene and n-butylnsodium.

For the purpose of comparison, an alkylsodium compound was reacted with  $\alpha$ -bromonaphthalene in petroleum ether.

A suspension of n-butylnsodium, prepared from 10 g. (0.032 mole) of di-n-butylmercury and 7 g. (0.3 g. atom) of sodium wire in two hundred ml. of low-boiling petroleum ether, was stirred with 13.5 g. (0.065 mole) of  $\alpha$ -bromonaphthalene. The reaction mixture was held at approximately 25° by a cold water bath. Aliquots were removed and carbonated. The yields of  $\alpha$ -naphthoic acid obtained are given in Table IV. The values given are only approximate as the insolubility of the organosodium compounds made the removal of an aliquot rather difficult.



Table IV

Yields of  $\alpha$ -Naphthoic Acid from  $\alpha$ -Bromonaphthalene  
and n-Butylsodium

<u>Time (min.)</u>	<u>Yield (%)</u>
2	17
4	20
8	28
16	28

Factors Affecting Metal-Metal Interconversion

Continuing the studies recently reported (172), other experiments were carried out to further determine the effect of various reactants in metal-metal interconversion. The experiments include reactions of other organoalkali compounds with organic compounds of lead and also of tin and mercury.

Tetraphenyllead and alkylolithium compounds.

To 0.06 mole of each of the organolithium compounds in 250 ml. of ether was added 0.0146 mole of finely powdered tetraphenyllead. The mixtures were stirred at room temperature and aliquots were removed and carbonated at suitable intervals. The yields of benzoic acid isolated are given in Table V.

Table V

Yields (%) of Benzoic Acid from Tetraphenyllead in Ether

<u>Time (hrs.)</u>	<u>C<sub>2</sub>H<sub>5</sub>Li</u>	<u>n-C<sub>3</sub>H<sub>7</sub>Li</u>	<u>n-C<sub>4</sub>H<sub>9</sub>Li</u>
0.5	45	40	38
1.0	56	45	45
2.0	58	48	49
4.0	61	54	52
7.0	65	59	54

Tetraphenyllead and methyllithium.

A solution of 0.54 mole of methyllithium in ether was stirred with 0.0126 mole of tetraphenyllead. At the end of three hours an aliquot was removed and carbonated. No benzoic acid was isolated from this aliquot. The remainder of the reaction mixture was carbonated after a reaction time of fifteen hours. The benzoic acid isolated corresponded to forty per cent cleavage of the tetraphenyllead.

Tetraphenyllead and phenylethynyllithium.

An ether solution of 0.11 mole of n-butyllithium was treated with an equivalent quantity of phenylacetylene. The resulting solution of phenylethynyllithium, C<sub>6</sub>H<sub>5</sub>C≡CLi, was diluted to 300 ml. and 0.02 mole of tetraphenyllead was added. The mixture was stirred at room temperature and aliquots were removed after five, seventeen, twenty-nine and sixty-seven hours. From the acidic material produced by carbonating these aliquots no benzoic acid could be isolated. The recovery of

tetraphenyllead was eighty-seven per cent.

Tetraphenyllead and n-butylsodium.

A suspension of n-butylsodium was prepared in 250 ml. of petroleum ether (b.p. 85-100°) by treating 0.032 mole of di-n-butylmercury with excess sodium metal. To this suspension was added 0.012 mole of tetraphenyllead. The mixture was stirred at room temperature and aliquots were removed and carbonated as usual. The yields of benzoic acid isolated, calculated on the basis of total cleavage of the organolead compound, are given in Table VI. Due to the difficulty of removing a representative sample of the reaction mixture, the yields are to be taken as approximate. Under these conditions tetraphenyllead is not appreciably affected by sodium metal (172).

Table VI

Yields of Benzoic Acid from Tetraphenyllead and  
n-Butylsodium

<u>Time (hrs.)</u>	<u>Yield (%)</u>
2	19
4	25
8	25
18	23

Tetraethyllead and phenyllithium.

To 450 ml. of ether containing 0.30 mole of phenyllithium

was added 0.067 mole of tetraethyllead. At the end of two hours an aliquot was removed and carbonated. The remainder of the reaction solution was carbonated at the end of twelve hours. No propionic acid was isolated from either portion nor was any phenyllead compound isolated from the recovered tetraethyllead. The recovery of tetraethyllead was ninety-five per cent.

Preferential cleavage of radicals from organolead compounds.

Since diphenyldi-*p*-tolyllead had given preferential cleavage of the *p*-tolyl group over the phenyl group with *n*-butyllithium (172) this reaction was extended to other unsymmetrical organolead compounds.

To 0.004 mole of each of the organolead compounds, dissolved in 65 ml. of ether, was added 0.004 mole of *n*-butyllithium in 10 ml. of ether. The solutions were stirred for ten minutes and then carbonated. No isolation of the organolead compounds formed was attempted. The compositions of the acid mixtures, as calculated from neutralization data, are given in Table VII.

Table VII

Preferential Cleavage of Radicals from Organolead Compounds

<u>Compound</u>	<u>Composition (%) of Acid Mixture</u>
$(C_6H_5)_3Pb(C_6H_4Cl-p)$	$C_6H_5CO_2H$ , 24; $p-ClC_6H_4CO_2H$ , 76.
$(C_6H_5)_2Pb(C_6H_4Cl-p)_2$	$C_6H_5CO_2H$ , 2; $p-ClC_6H_4CO_2H$ , 98.
$(C_6H_5)_2Pb(C_6H_4CH_3-p)_2$	$C_6H_5CO_2H$ , 21; $p-CH_3C_6H_4CO_2H$ , 79.

Tetraphenyltin and n-butyllithium.

A solution of 0.05 mole of n-butyllithium in ether was added to a solution of 0.003 mole of tetraphenyltin in an equal volume of benzene. This solution was refluxed for twenty-four hours at 55° and then carbonated. The products were isolated by customary procedures. Tetra-n-butyltin (b.p.<sub>10</sub> 140-144°) was obtained in eighty-one per cent yield. A forty-eight hour run yielded eighty-eight per cent of the alkyltin compound, which was identified by its refractive index and density. The yields of benzoic acid were thirty-six per cent and twenty-one per cent, respectively.

A similar reaction was run using benzene as solvent (no ether present). Carbonation yielded only a trace of benzoic acid.

Another experiment, using petroleum ether (b.p. 85-100°) as solvent, yielded no benzoic acid subsequent to carbonation and hydrolysis after heating for twenty-four hours at 85°.

Tetraphenyltin and benzylnsodium.

A suspension of benzylnatrium prepared (150) from 4.1 g. of chlorobenzene and 1.4 g. of sodium in 50 ml. of toluene was stirred with 0.004 mole of tetraphenyltin for twenty-four hours at 107°. Carbonation produced no benzoic acid and ninety per cent of the tin compound was recovered.

Tetra-p-chlorophenyltin and n-butyllithium.

A solution of 0.004 mole of tetra-p-chlorophenyltin in 65 ml. of ether was stirred with 0.004 mole of n-butyllithium in 10 ml. of ether for ten minutes and then carbonated. The p-chlorobenzoic acid obtained corresponded to seventy-two per cent cleavage based on the removal of one group or to eighteen per cent of the tin compound used. No isolation of the possible tin compounds formed was attempted.

In a similar experiment, run in benzene-petroleum ether (2:1) for four hours, the yield of p-chlorobenzoic acid was only forty per cent as compared to the seventy-two per cent in ten minutes in ether. After eight hours the yield of acid corresponded to forty-five per cent cleavage.

Tetra-p-chlorophenyltin and isomeric butyllithium compounds.

To determine the relative reactivities of the various isomeric butyllithium compounds in metal-metal interconversion these four compounds were reacted with tetra-p-chlorophenyltin in low-boiling petroleum ether. This solvent was

necessary to avoid complicating side reactions.

Solutions of each of the butyllithium compounds were prepared in petroleum ether (b.p. 28-38°) and these were diluted to 0.10 molar. To 200 ml. (0.02 mole) of each of these solutions was added 0.005 mole of tetra-*p*-chlorophenyltin. The mixtures were stirred at room temperature and aliquots were removed and carbonated. In Table VIII are given the yields of *p*-chlorobenzoic acid obtained. The yields are calculated on the basis of complete cleavage of the organotin compound.

Table VIII

Yields (%) of *p*-Chlorobenzoic Acid from  
Tetra-*p*-chlorophenyltin

<u>Time (hrs.)</u>	<u><i>n</i>-C<sub>4</sub>H<sub>9</sub>Li</u>	<u><i>iso</i>-C<sub>4</sub>H<sub>9</sub>Li</u>	<u><i>s</i>-C<sub>4</sub>H<sub>9</sub>Li</u>	<u><i>t</i>-C<sub>4</sub>H<sub>9</sub>Li</u>
0.5	6	8	5	0
1.0	13	12	9	0
2.0	19	19	16	0
4.0	26	19	22	0

Tetra-*p*-chlorophenyltin with phenyl- and methyllithium.

In order to compare the reactivities of phenyl- and methyllithium with the other lithium compounds mentioned above, 0.005 mole of tetra-*p*-chlorophenyltin was added to 0.02 mole of an ether solution of phenyllithium and methyllithium. The solutions were stirred at room temperature for fifteen minutes and then carbonated. The yield of *p*-chloro-

benzoic acid isolated from the phenyllithium reaction mixture was 53%; the yield in the case of methyllithium was 55%.

Dibenzylmercury and methyllithium.

A solution of 0.01 mole of dibenzylmercury in 200 ml. of ether was stirred with 0.02 mole of methyllithium in 100 ml. of ether. Aliquots were removed and carbonated as usual. The yields of phenylacetic acid, calculated on the basis of total cleavage of the organomercury compound, are given in Table IX.

Table IX

Yields of Phenylacetic Acid from Dibenzylmercury and Methyllithium

<u>Time (min.)</u>	<u>Yield (%)</u>
0.5	79
5.0	77
30.0	73

Dibenzylmercury with *n*- and *t*-butyllithium.

To solutions of 0.005 mole of dibenzylmercury in 150 ml. of benzene were added separately 0.01 mole of *n*- and *t*-butyllithium in 50 ml. of low-boiling petroleum ether. The solutions were stirred and aliquots were removed and carbonated. The yields of phenylacetic acid obtained are given in Table I. The yields are calculated on the basis of total cleavage of the dibenzylmercury.



Table X

Yields (%) of Phenylacetic Acid from Dibenzylmercury with  
n- and t-Butyllithium

<u>Time (min.)</u>	<u>n-C<sub>4</sub>H<sub>9</sub>Li</u>	<u>t-C<sub>4</sub>H<sub>9</sub>Li</u>
2	53	15
5	50	15
15	40	15

Diphenylmercury with n- and t-butyllithium.

Experiments, similar to those above, were run replacing the dibenzylmercury by diphenylmercury. The yields of benzoic acid obtained are given in Table XI. The yields are calculated on the same basis as before; total cleavage of the organomercury compound.

Table XI

Yields (%) of Benzoic Acid from Diphenylmercury with n- and  
t-Butyllithium

<u>Time (min.)</u>	<u>n-C<sub>4</sub>H<sub>9</sub>Li</u>	<u>t-C<sub>4</sub>H<sub>9</sub>Li</u>
2	65	10
5	65	13
15	62	13

Rates of cleavage by n-butyllithium.

A comparison of the rates of cleavage of tetraphenyllead tetraphenyltin and tetra-o-tolyllead by n-butyllithium was made by adding equivalent amounts of n-butyllithium to solutions of each of the above-mentioned compounds, stirring for

thirty minutes and then carbonating. Check runs were made in each case. The results of this series are given in Table XII. The percentages are, as usual, based on the quantities of acids isolated.

Table XII

Rates of Cleavage by n-Butyllithium

<u>Compound</u>	<u>% Cleavage</u>
Tetraphenyllead	30
Tetraphenyltin	45
Tetra- <u>o</u> -tolyllead	3

Miscellaneous

Attempted interconversions of triphenyl-p-bromophenyllead.

Attempts to convert the p-bromophenyl radical in triphenyl-p-bromophenyllead to the p-carboxyphenyl radical by halogen-metal interconversion followed by carbonation have thus far been unsuccessful.

To a benzene-petroleum ether solution of 0.007 mole of triphenyl-p-bromophenyllead was added 0.015 mole of t-butyllithium in petroleum ether. The solution was stirred at room temperature. An aliquot, removed after fifteen minutes, gave no lead-containing acid following carbonation and hydrolysis. The result was the same at the end of an hour.

The experiment was repeated using s-butyllithium in place

of the t-butyllithium. Here, also, no lead-containing acid was isolated. Recovery of the triphenyl-p-bromophenyllead averaged above ninety per cent.

Addition of isomeric butyllithium compounds to isostilbene.

In order to compare the relative reactivities of the isomeric butyllithium compounds as regards their addition to ethylenic linkages, the addition to 1,1-diphenylethylene (isostilbene) was studied. The extent of reaction was estimated by carbonation and hydrolysis. The weights of acid obtained were made the basis of the calculation of per cent of addition. This method is unsatisfactory since the acids produced are not pure and may consist of mixtures. Further work must be done on this reaction before definite conclusions may be safely drawn.

Equimolar quantities of isostilbene and n-, iso, and s-butyllithium were mixed separately in benzene-petroleum ether solution. Another run was made using s- and t-butyllithium with isostilbene in petroleum ether alone. The results of these experiments are given in Table XIII.

Table XIII

Addition of Isomeric Butyllithium Compounds to Isostilbene  
(%)

<u>Time (hrs.)</u>	<u>n-BuLi</u>	<u>iso-BuLi</u>	<u>s-BuLi</u>	<u>t-BuLi</u>
(benzene-petroleum ether)				
8	12	13	82	
48	35	37	82	
(petroleum ether)				
8			13	7
48			90	18

Cleavage of diphenyldi-p-chlorophenyllead by hydrogen chloride.

A solution of 0.05 mole of diphenyldi-p-chlorophenyllead in benzene was treated with dry hydrogen chloride gas until no further precipitate formed. The addition of gas was continued for thirty minutes after this stage was reached. The precipitate was then dried and analyzed for lead. The calculated percentages of lead in each of the possible lead compounds formed are as follows:

$(C_6H_5)_2PbCl_2$	Pb = 47.92%
$(C_6H_5)(p-ClC_6H_4)PbCl_2$	Pb = 44.37%
$(p-ClC_6H_4)_2PbCl_2$	Pb = 41.32%

Anal: Pb, Found: 43.18%, 43.30%

The above conditions are those which usually lead to removal of two groups from an  $R_4Pb$  compound. On this basis the analysis corresponds to a mixture of  $R_2PbCl_2$  compounds

with the p-chlorophenyl group being present in greater quantity than the phenyl group.

## DISCUSSION

The organolithium compounds, on the whole, are most conveniently prepared by the reaction of organic bromides or chlorides with lithium in diethyl ether. The more reactive alkyllithium compounds, however, may be conveniently and more satisfactorily prepared by replacing the diethyl ether with low-boiling petroleum ether as the solvent for the reaction. Not only does this solvent permit higher yields to be obtained but the resulting solutions of organolithium compounds may be freed of inorganic by-products by the use of a simple, easily constructable filtration apparatus. The advantages offered by this method of preparation have been outlined previously (see page 33). The use of petroleum ether as a solvent has permitted the preparation of a new organolithium compound, t-butyllithium. All types of saturated alkyllithium compounds are now known, namely those in which the metal atom is attached to a primary, to a secondary and to a tertiary carbon atom. The rapid cleavage of ether by t-butyllithium shows why previous attempts to prepare this compound in ether were predestined to failure. The fact that iso-propyl- and s-butyllithium also cleave ether fairly rapidly explains the unsatisfactory yields of these compounds when prepared in diethyl ether solution. Unfortunately, the

aryllithium compounds and methyllithium are insoluble in petroleum ether and so no improvement in their preparation is possible by using this solvent.

The advantages of being able to use clear, water-white solutions of alkyllithium compounds are numerous. The absence of interfering by-products and a knowledge of the actual concentration of organometallic compound are among the more important of these. These are especially significant in rate studies and determinations of relative reactivities as will be discussed later.

A study of the factors affecting halogen-metal interconversions has shown many of these to be quite general, a fact which has been used to advantage in subsequent studies. The most important of these general factors, with a given organic halide and alkyllithium compound, is the solvent used. For maximum yields of interconversion product the use of petroleum ether is recommended, as this solvent allows a satisfactory rate of halogen-metal interconversion in most cases but seemingly inhibits other reactions such as metalation and metal-metal interconversion. Where halogen-metal interconversion is the desired reaction with a compound which also has other functional groups which react with organolithium compounds, it is often advisable to use diethyl ether as solvent and allow the reaction to proceed for a very short time at a low temperature. This method has been used

successfully with compounds like o-bromonitrobenzene, bromo- and iodobenzoic acids (153) and with bromine compounds of pyridine and quinoline (154).

In the absence of other functional groups the most interconversion is obtained with compounds having the lithium attached to a secondary carbon atom. Either iso-propyl- or s-butyllithium may be used, the s-butyllithium being slightly more effective in this case. The use of moderate concentrations is recommended to obtain good yields of interconversion products in reasonable lengths of time. Although the polar solvents, such as the ethers, give the most rapid rates of halogen-metal interconversion, the use of these solvents is limited. Reactions in which the organometallic compounds formed combine instantly with the desired reactants may be run in these solvents. For example, if the desired reaction is that between p-chlorophenyl-lithium and a compound like benzonitrile, the reaction could be carried out in the following manner. To an ether solution of n-butyllithium is added an equivalent quantity of p-bromochlorobenzene followed, after a short time (ca. ten minutes), by the calculated quantity of benzonitrile. Reactions proceeding at a lower rate should not be run in ether because the coupling reaction would probably be more rapid and poor yields of the desired compounds would be obtained.



The kind of organolithium compound used has an important effect as has been demonstrated by the studies with  $\alpha$ -bromophthalene. Under conditions where n-propyllithium gives a ninety-five per cent interconversion, only a trace of interconversion product is obtained with methyllithium. Methyllithium is recommended as a reagent of choice for the metalation of some bromo compounds where halogen-metal interconversion is not desired. This recommendation has been substantiated by the metalation of several bromodiphenyl ethers (212).

The metal-metal interconversion reaction seems quite general. Cases are known involving organic compounds of at least one metal in Groups II, III, IV and V of the Periodic System. Whether or not the reaction is universal remains to be established. It is likely so, however, insofar as true organometallic compounds are concerned.

In the investigations reported here the most outstanding factor was the effect of the solvent. The effect of the nature of the solvent is more diverse than in the case of halogen-metal interconversion. The latter reaction took place in all the solvents examined, but in the former case reaction was often completely inhibited. This again illustrates the important role played by solvents in organic

212. Unpublished studies by W. Langham, R. Q. Brewster and H. Gilman.

reactions and emphasizes the fact that diethyl ether is still one of the best solvents for reactions of organometallic compounds, although it is cleaved more or less rapidly by many such compounds. Diethyl ether is not indispensable, however, for all the types of interconversion can be carried out without using this solvent.

An interesting observation made during the earlier phases of this study of metal-metal interconversion was that different organic radicals were cleaved from the metallic atom at different rates. Some subsequent experiments were made to determine the order in which some of these radicals were cleaved. Kharasch and his coworkers have extensively studied the order of cleavage of radicals from unsymmetrical organomercury compounds by hydrogen chloride. Since a review of this work has been made recently (213), no extensive review will be given here, it being sufficient to say that the radical which was cleaved more readily from a compound like  $RHgR'$  was considered to be the more "electronegative". On this basis Kharasch has set up his so-called "Electronegativity Series" of organic radicals and has been able to correlate this series with data concerning several different kinds of reactions. There are also several cases where such correlation does not exist. The order of cleavage of radicals

213. H. L. Yablunsky, Doctoral Dissertation, Iowa State College, 1940.

in metal-metal interconversions is one of these and is the only one which will be discussed as pertinent to this thesis. In the Kharasch series, the order of decreasing "electronegativity" for the radicals examined in this work is as follows: o-tolyl > p-tolyl > phenyl > p-chlorophenyl. In the metal-metal interconversion reaction between unsymmetrical and symmetrical compounds of lead and tin the order of decreasing ease of cleavage was p-chlorophenyl > p-tolyl > phenyl > o-tolyl. This latter order is, except for the phenyl, the reverse of the former order. However, in similar reactions with bismuth compounds, tri-p-tolylbismuth is cleaved less rapidly than triphenylbismuth (214). Apparently, in determining the order of cleavage of radicals from organometallic compounds, factors other than the "electronegativity" of the radical are involved. Such variables as solubility, nature of the central atom holding the radicals, and the cleaving agent may play important roles in determining such orders. Steric factors very probably play a part, as is seen in the low rate of interconversion of tetra-o-tolyllead with n-butyllithium and of dibenzylmercury and diphenylmercury with t-butyllithium.

Various attempts have been made to determine the relative reactivities of organometallic compounds. These attempts have been successful insofar as each is concerned, and some

214. Unpublished studies by H. L. Yablunsky.

success has been had in comparing various orders of reactivity with each other. In most cases, however, exact correlation of one series with another is not possible. For example, if a series of organometallic compounds is arranged in the order of increasing rates of reaction of these compounds with some functional group, this series can be extended to other reactions only with caution and often-times must undergo extensive revision. General orders of reactivity usually hold and exceptions are most often encountered when comparing two compounds of almost equal reactivity.

The determination of relative reactivities is sometimes made difficult because of interfering side reactions. In fact, these side reactions may obscure the true reactivities of some compounds under consideration.

In general, the organolithium compounds have the relative reactivities expected from the position of lithium in the periodic system. They are less reactive than the corresponding sodium compounds and more reactive than the corresponding Grignard reagents (127, 128). This general order of reactivity has been well established by several investigators and need not be considered further (112, 127, 128, 129, 191, 207, 215).

215. Gilman and Young, J. Am. Chem. Soc., 57, 1121 (1935).

A comparison of the relative reactivities of the organolithium compounds themselves is not so easily made, for several apparently anomalous reactions are known. Before a general comparison is made it is necessary to summarize the relative reactivities in various kinds of reactions shown by these compounds.

The reaction with functional groups, like the carbonyl or nitrile, is so rapid under ordinary circumstances that no clean-cut series can be obtained with closely related compounds. In other types of reaction, however, significant differences in reaction rates are often obtained. Thus, in metalation reactions these differences can be estimated by carbonation and isolation of the resulting acids. In this manner the order of decreasing reactivity of the isomeric butyllithium compounds toward dibenzofuran in petroleum ether has been found to be t-butyl- > s-butyl- > iso-butyl- = n-butyllithium (216).

The relative reactivities of the organolithium compounds in halogen-metal interconversion have also been determined by measuring the amounts of  $\alpha$ -naphthoic acid produced from  $\alpha$ -bromonaphthalene following carbonation and hydrolysis after various time periods. In ether solution the normal alkyl-lithium compounds and phenyllithium gave the following order of decreasing reactivity as determined from the amounts of 216. Unpublished studies by O. Baine.

$\alpha$ -naphthoic acid formed under comparable conditions: n-propyl > ethyl > n-butyl > n-amyl > phenyl > methyl. In petroleum ether the following order was obtained with the alkyl compounds (except methyllithium): s-butyl > iso-propyl > t-butyl > n-butyl = iso-butyl > n-propyl.

In metal-metal interconversion the order obtained with tetraphenyllead was: ethyl > n-propyl > n-butyl > methyl > phenyl-ethynyl. With tetra-*p*-chlorophenyltin in ether the order was: n-butyl > methyl = phenyl, and in petroleum ether: n-butyl = iso-butyl = s-butyl > t-butyl.

These facts may be used to predict the relative effectiveness of these compounds in other related reactions. The most powerful organolithium compound for metalation is t-butyllithium. That is, t-butyllithium will be found most effective for metalating; but, unfortunately, can be used only in an inert solvent like petroleum ether. Its use will thus be limited to those nuclei which give no metalation with n-butyllithium in ether solution since this latter compound metalates dibenzofuran in ether to a greater extent than does t-butyllithium in petroleum ether in the same length of time. s-Butyllithium is a better metalating agent than n-butyllithium in petroleum ether and is equaled in reactivity by iso-propyllithium. The uses of these compounds for metalations will be limited to those nuclei which are metalated by these compounds in ether solution more rapidly

than the ether is cleaved by these compounds. Studies now in progress must be completed before this limitation will be clearly defined. In general, then, the relative reactivity in metalation decreases as the lithium atom is attached to a tertiary, to a secondary and to a primary carbon atom, respectively.

In halogen-metal interconversion the order of reactivity is not the same as that observed in metalation. Here the s-butyl- and iso-propyllithium are most effective with  $\alpha$ -bromonaphthalene. This may be due, in part, to the greater reactivity of the t-butyl compound in coupling reactions which always accompany halogen-metal interconversions to a greater or lesser extent (see page 78). This is another illustration of the difficulty of determining relative reactivities when side reactions take place simultaneously with the desired reaction.

In metal-metal interconversion the order of reactivity is the reverse of that expected from the Kharasch series with the exception of methyllithium which seems definitely anomalous in nearly all its reactions. Many facts show this decidedly low reactivity of methyllithium. Among these may be mentioned its preparation in good yield from methyl iodide, the lack of halogen-metal interconversion with  $\alpha$ -bromonaphthalene, its slow cleavage of tetraphenyllead in ether solution, its stability in ether solution, and, finally, the low

yields of metalation products obtained in many cases. This low reactivity has some distinct advantages, however. Methyl-lithium has proved to be an excellent reagent for metalating compounds containing bromine atoms (212), and it has been used to effect monometalation of a compound where n-butyl-lithium gives dimetalation (217). The failure of t-butyl-lithium to undergo metal-metal interconversion with tetra-p-chlorophenyltin may be due to steric factors. With diphenyl-mercury and dibenzylmercury the extent of interconversion was much less than that obtained with n-butyllithium, further strengthening this explanation.

217. Unpublished studies by C. G. Stuckwisch.



### SUMMARY

A review of the chemistry of the organolithium compounds has been made.

A study of the important factors affecting halogen-metal interconversion has been carried out.

A systematic study of metal-metal interconversion reactions of organometallic compounds has been started and groundwork for further study in this important field has been laid.

A new organolithium compound, t-butyllithium, has been prepared, completing the series of saturated alkylolithium compounds in which the lithium atom is attached to a primary, secondary and tertiary carbon atom, respectively.

More refined techniques for the preparation and manipulation of alkylolithium compounds have been developed.

The relative reactivities of various organometallic compounds in several types of reaction have been determined.